

CHAPTER 20

PULMONARY DISEASE

INTRODUCTION

Background

Pulmonary dysfunction and overt pulmonary disease are not recognized clinical entities resulting from exposure to chlorophenols or 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD).

Little research has been done on possible pulmonary effects of TCDD or other dioxin-related compounds. Animal studies have been limited to in vitro determination of the binding of TCDD to lung tissue components. Tissue obtained from the lung included cytosol from rat lung, which showed a high-affinity, low-capacity binding complex for TCDD.¹ Human lung cytosols from normal lung tissue taken from 53 adults were used to establish the Ah receptor for TCDD and other polycyclic aromatic hydrocarbons. Indications were obtained of a genetic basis for Ah receptor levels for these compounds (implying a genetic basis for chemically induced cancer).² Other studies have focused on the mechanism of cytochrome P-450 induction in rabbit pulmonary tissue; these results have not been extrapolated to possible health effects.³⁻⁵

In humans, lung cancers have been associated with MCPA [(2,4-dichlorophenoxy)-acetic acid] and 2,4,5-T exposures in a Danish study of phenoxy herbicides manufacturing workers, but other pulmonary diseases were not investigated.^{6,7}

Acute exposure to chlorophenols, phenoxy herbicides, and TCDD have caused the traditional acute symptoms of cough, nasal/lung irritation, shortness of breath, and, occasionally, bronchitis. These symptoms have been noted almost exclusively in industrial workers and not in individuals experiencing casual contact. Long-term sequelae arising from the acute symptom stage in ill individuals have not been generally known because of minimal followup and surveillance of the pulmonary symptoms.

Only one contemporary morbidity study has attributed pulmonary dysfunction to phenoxy herbicide and TCDD exposure.⁸ The percent abnormal pulmonary parameters of forced expiratory volume (FEV), forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁)/FVC ratio, and forced mid-expiratory flow rate were significantly higher in exposed workers who currently smoke than in nonexposed workers who smoke. In considerable contrast, these test parameters were essentially equal in nonsmokers and former smokers of both the exposed and nonexposed groups. The effect of current smoking persisted after a logistic regression analysis adjusting for pack-years of cigarette smoking. Adjusted means of the test parameters FEV, FVC, and FEV₁/FVC also showed significant differences for current smokers but not for nonsmokers or former smokers.

Further, due to the profound effect of smoking on pulmonary function, great emphasis must be placed on the collection of highly accurate, detailed, and validated smoking data as an adjustment variable.

Baseline Summary Results

The 1982 Baseline examination explored historical pulmonary disease by questionnaire and active pulmonary function by standardized spirometric technique. These areas were of significant interest because of suggested operational inhalation of Herbicide Orange by all Ranch Hand flying crewmen as well as ground maintenance personnel.

The questionnaire revealed no group differences for historical diagnoses of tuberculosis and fungal infections, pneumonia, cancer, or chronic sinusitis and upper respiratory disease. At the physical examination, the unadjusted means for FEV₁ (percent predicted), FVC, and the FEV₁/FVC ratio were almost identical between the Ranch Hands and Comparisons. Adjusted mean values were not calculated due to significant interactions (group-by-age for FEV₁ and FVC; group-by-smoking with FEV₁/FVC).

Detailed exposure analyses showed two significant associations in the enlisted flyer and enlisted groundcrew strata, but neither was indicative of a linear dose response. Attempts to adjust the means of the pulmonary function values for age and smoking revealed several interactions, but essentially negative results.

Overall, there were no pulmonary disease or pulmonary function data or associations of concern.

1985 Followup Study Summary Results

Because of the essentially negative pulmonary analyses from the Baseline examination, pulmonary function (spirometric) studies were not performed during the 1985 followup examination. Collection of pulmonary data was limited to a questionnaire history of respiratory disease, physical examination of the thorax and lungs, and pulmonary abnormalities detected on a routine chest x ray. Mortality due to respiratory disease was also evaluated.

There were no significant group differences found for reported history of asthma, bronchitis, pleurisy, or tuberculosis based on the unadjusted analyses. Adjustments for age and lifetime smoking did not alter the findings of group similarity, although there was a significant group-by-lifetime smoking interaction for pleurisy and for tuberculosis.

Similarly, there were no significant group differences in the unadjusted analyses for the radiological and clinical respiratory findings of thorax and lungs, asymmetrical expansion, hyperresonance, dullness, wheezes, rales, and x-ray interpretations. These findings were supported by the adjusted analyses, although there was a group-by-age interaction for rales.

The exposure index analyses revealed no consistent dose-response pattern.

Parameters of the 1987 Pulmonary Assessment

Dependent Variables

Questionnaire, physical examination, and laboratory data were used in the pulmonary assessment for the 1987 followup.

Questionnaire Data

In the self-administered family and personal history section, each study participant was asked whether he had ever experienced the following conditions: asthma, bronchitis, pleurisy, pneumonia, and tuberculosis. These five variables, based on self-reported and unverified information, were analyzed as a measure of the pulmonary health status of each participant.

No participants were excluded for medical reasons from the analysis of these variables.

Physical Examination Data

Part of the pulmonary assessment was based on the results of the physical examination of the thorax and lungs, and pulmonary abnormalities detected on a routine chest x ray. The following seven variables from the radiologic and physical examinations were analyzed in the pulmonary assessment: asymmetrical expansion, hyperresonance, dullness, wheezes, rales, thorax and lung abnormalities (a composite variable including all of the previous conditions), and x-ray interpretation. These variables were coded as normal/abnormal for x-ray interpretation, and as yes/no for the other variables.

No participants were excluded for medical reasons from the analysis of these variables.

Laboratory Examination Data

The 1987 assessment included the analysis of pulmonary physiologic data collected during the physical examination employing standard spirometric techniques. Numerous indices were derived including (1) FVC, a measurement of the amount of air in liters expelled from maximum inspiration to full expiration; (2) FEV, in liters, an index derived from the FVC that quantifies the amount of air expelled at 1 second (FEV₁), 2 seconds (FEV₂), and 3 seconds (FEV₃); and (3) forced expiratory flow (FEFmax), an index of peak instantaneous flow in liters per second during a forced expiration. The values used for these variables were the percentages of predicted values rather than the actual volume or flow rate. In addition, the ratio of FEV₁ to FVC was calculated as an index reflective of obstructive airways disease. For these indices, lower values indicate greater compromise in the lung function. These variables were analyzed as continuous variables. For the ratio of observed FEV in 1 second to observed FVC, the natural logarithm of 1 minus the ratio transformation was used. Loss of vital capacity and obstructive abnormality were classified as none, mild, moderate, or severe and were analyzed as part

of the 1987 pulmonary assessment. Results judged to be between none and mild were classified as mild for all analyses. A similar methodology was used for results between mild and moderate, and between moderate and severe, where the next most abnormal category was applied. Due to the low frequencies in the moderate and severe categories, these two categories were combined in the analysis.

As a guide for determining abnormal pulmonary function, readings below the 95th percentile are considered abnormal for the FVC and FEV_1 . For men above 36 years of age, the corresponding percent of predicted is 74 percent for the FVC and 73 percent for the FEV_1 . An FVC or FEV_1 below 40 percent of predicted is considered severely impaired, as recommended by the American Thoracic Society. The division between mild, moderate, and severe impairment is arbitrarily defined by dividing the interval between severe impairment and the lower limit of normal into two equal bands. That is, the cutpoint between mild and moderate impairment is at 57 percent of the predicted value. Although the other spirometric indices (FEV_2 , FEV_3 , FEFmax, FEV_1/FVC) and the appearance of the flow volume curve are useful to the physician interpreting the test, there are no good statistical data to support arbitrary lower limits of normal or cutpoints to classify impairment as mild, moderate, or severe.

No participants were excluded for medical reasons from the analysis of these variables.

Covariates

The effects of age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history were examined in the assessment of pulmonary function, both in pairwise associations with the dependent variables and in adjusted statistical analyses. Current cigarette smoking and lifetime cigarette smoking history were based on self-reported questionnaire data.

In the discussion of the smoking covariates, the different classes of current cigarette smoking are (1) nonsmokers (those who never smoked cigarettes, shown as 0-Never in Table 20-1); (2) former smokers (those who used to smoke cigarettes but currently do not, shown as 0-Former); (3) moderate smokers (those who smoke, on the average, more than 0 but not more than 20 cigarettes per day); and (4) heavy smokers (those who smoke, on the average, more than 20 cigarettes per day). The categories of lifetime cigarette smoking history are (1) 0 pack-years or nonsmokers; (2) greater than 0 but not more than 10 pack-years, which will be referred to as moderate smokers; and (3) greater than 10 pack-years or heavy smokers.

Age and lifetime cigarette smoking history were used in the continuous form for modeling purposes in all general linear models and logistic regression analyses; these variables were discretized for use in log-linear analyses. These covariates were also discretized for presentation purposes (e.g., dependent variable-covariate associations and interaction summaries). Current cigarette smoking was discretized in adjusted analyses for eight dependent variables (asthma, bronchitis, pleurisy, pneumonia, rales, x ray, loss of vital capacity, and obstructive abnormality) and was used in its continuous form for adjusted analyses of the other dependent variables.

Several relationships between group and the covariates and among covariates are of special interest in interpreting subsequent analyses. As discussed in Chapter 2, Ranch Hands currently smoke more cigarettes per day,

on the average, than Comparisons ($p=0.014$). Enlisted flyers and enlisted groundcrew smoke more cigarettes per day (means of 11.1 and 10.4, respectively) than officers (4.7). In terms of lifetime cigarette smoking history, enlisted flyers have, on the average, smoked more (a mean of 19.2 pack-years) than either the enlisted groundcrew or officers (14.0 pack-years and 12.8 pack-years, respectively). Associations for both smoking variables with occupation are significant ($p<0.001$). Nonblacks also have a stronger history of cigarette smoking than Blacks.

Relation to Baseline and 1985 Followup Studies

In general, the same variables that were analyzed in the 1987 followup study were analyzed at Baseline, although a slightly different classification of reported pulmonary disease was used in the Baseline analyses. In the 1985 followup, the pulmonary physiology data were not collected. The questionnaire and physical examination data analyzed in the 1987 followup were analyzed for the 1985 followup.

In the longitudinal analysis, group differences in the changes from Baseline in the ratio of observed FEV in 1 second to observed FVC were analyzed.

Statistical Methods

Table 20-1 summarizes the statistical analyses performed for the 1987 pulmonary assessment. The first part of this table lists the dependent variables analyzed, the source of the data, the form of the data (discrete/continuous), cutpoints (if applicable), the candidate covariates, and the statistical methods. The basic statistical analysis methods used are described in Chapter 7. The second part of this table provides a further description of candidate covariates examined. Abbreviations are used extensively in the body of the table and are defined in footnotes.

Due to the low number of abnormalities, adjusted analyses of tuberculosis, asymmetric expiration, and dullness were not conducted.

Although no participants were excluded for medical reasons in the pulmonary assessment, dependent variable data were missing in some cases. The number of participants with missing data is provided in Table 20-2 by group and variable.

RESULTS

Ranch Hand and Comparison Group Contrast

Questionnaire Variables

The results of the unadjusted and adjusted Ranch Hand and Comparison group contrasts for the questionnaire variables of the pulmonary assessment are summarized in Tables 20-3 and 20-4, respectively. Table Q-1 of Appendix Q

TABLE 20-1.

Statistical Analysis for the Pulmonary Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Asthma	Q-SR	D	No Yes	AGE RACE OCC CSMOK PACKYR	UC: FT AC: LR CA: CS, FT UE: CS, FT AE: LR
Bronchitis	Q-SR	D	No Yes	AGE RACE OCC CSMOK PACKYR	UC: FT AC: LR CA: CS, FT UE: CS, FT AE: LR
Pleurisy	Q-SR	D	No Yes	AGE RACE OCC CSMOK PACKYR	UC: FT AC: LR CA: CS, FT UE: CS, FT AE: LR
Pneumonia	Q-SR	D	No Yes	AGE RACE OCC CSMOK PACKYR	UC: FT AC: LR CA: CS, FT UE: CS, FT AE: LR
Tuberculosis	Q-SR	D	No Yes	--	UC: FT UE: CS, FT
Thorax and Lung Abnormalities	PE	D	No Yes	AGE RACE OCC CSMOK PACKYR	UC: FT AC: LR CA: CS, FT UE: CS, FT AE: LR
Asymmetric Expansion	PE	D	No Yes	--	UC: FT UE: CS, FT
Hyperresonance	PE	D	No Yes	AGE RACE OCC CSMOK PACKYR	UC: FT AC: LR CA: CS, FT UE: CS, FT AE: LR

TABLE 20-1. (continued)

Statistical Analysis for the Pulmonary Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Dullness	PE	D	No Yes	--	UC: FT UE: CS, FT
Wheezes	PE	D	No Yes	AGE RACE OCC CSMOK PACKYR	UC: FT AC: LR CA: CS, FT UE: CS, FT AE: LR
Rales	PE	D	No Yes	AGE RACE OCC CSMOK PACKYR	UC: FT AC: LR CA: CS, FT UE: CS, FT AE: LR
X-Ray Interpretation	PE	D	Normal Abnormal	AGE RACE OCC CSMOK PACKYR	UC: FT AC: LR CA: CS, FT UE: CS, FT AE: LR
Forced Vital Capacity (PVC) (percent of predicted)	LAB	C	--	AGE RACE OCC CSMOK PACKYR	UC: TT AC: GLM CA: GLM, CC UE: GLM, TT AE: GLM
Forced Expiratory Volume in 1 Second (FEV ₁) (percent of predicted)	LAB	C	--	AGE RACE OCC CSMOK PACKYR	UC: TT AC: GLM CA: GLM, CC UE: GLM, TT AE: GLM
Forced Expiratory Volume in 2 Seconds (FEV ₂) (percent of predicted)	LAB	C	--	AGE RACE OCC CSMOK PACKYR	UC: TT AC: GLM CA: GLM, CC UE: GLM, TT AE: GLM
Forced Expiratory Volume in 3 Seconds (FEV ₃) (percent of predicted)	LAB	C	--	AGE RACE OCC CSMOK PACKYR	UC: TT AC: GLM CA: GLM, CC UE: GLM, TT AE: GLM

TABLE 20-1. (continued)

Statistical Analysis for the Pulmonary Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Forced Expiratory Flow Maximum (FEFmax) (percent of predicted)	LAB	C	--	AGE RACE OCC CSMOK PACKYR	UC:TT AC:GLM CA:GLM,CC UE:GLM,TT AE:GLM
Ratio of Observed FEV ₁ to Observed FVC	LAB	C	--	AGE RACE OCC CSMOK PACKYR	UC:TT AC:GLM CA:GLM,CC UE:GLM,TT AE:GLM L:RM
Loss of Vital Capacity	LAB	D	None Mild Moderate/ Severe	AGE RACE OCC CSMOK PACKYR	UC:CS,FT AC:LL CA:CS UE:CS,FT AE:LL
Obstructive Abnormality	LAB	D	None Mild Moderate/ Severe	AGE RACE OCC CSMOK PACKYR	UC:CS,FT AC:LL CA:CS UE:CS,FT AE:LL

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥ 1942 Born 1923-1941 Born ≤ 1922
Race (RACE)	MIL	D	Nonblack Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew

TABLE 20-1. (continued)

Statistical Analysis for the Pulmonary Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Current Cigarette Smoking (CSMOK)(cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0-20 >20
Lifetime Cigarette Smoking History (PACKYR) (pack-years)	Q-SR	D/C	0 >0-10 >10

Abbreviations:

Data Source: LAB--1987 SCRF laboratory results
MIL--Air Force military records
PE--1987 SCRF physical examination
Q-SR--1987 NORC questionnaire (self-reported)

Data Form: C--Continuous analysis only
D--Discrete analysis only
D/C--Appropriate form for analysis (either discrete or continuous)

Statistical Analyses: UC--Unadjusted core analyses
AC--Adjusted core analyses
CA--Dependent variable-covariate associations
UE--Unadjusted exposure index analyses
AE--Adjusted exposure index analyses
L--Longitudinal analyses

Statistical Methods: CC--Pearson's product moment correlation coefficient
CS--Chi-square contingency table test
FT--Fisher's exact test
GLM--General linear models analysis
LL--Log-linear models analysis
LR--Logistic regression analysis
RM--Repeated measures analysis
TT--Two-sample t-test

TABLE 20-2.

Number of Participants With Missing Data for the
Pulmonary Assessment by Group

Variable	Analysis Use	Group		Total
		Ranch Hand	Comparison	
Asthma	DEP	0	1	1
Bronchitis	DEP	1	1	2
Pleurisy	DEP	2	3	5
Pneumonia	DEP	0	1	1
Tuberculosis	DEP	0	1	1
X-Ray Interpretation	DEP	4	4	8
FVC	DEP	2	0	2
FEV ₁	DEP	2	0	2
FEV ₂	DEP	2	0	2
FEV ₃	DEP	2	0	2
FEFmax	DEP	2	0	2
Ratio of Observed FEV ₁ to Observed FVC	DEP	2	0	2
Loss of Vital Capacity	DEP	2	0	2
Obstructive Abnormality	DEP	2	0	2

Abbreviations: DEP--Dependent variable (missing data)

TABLE 20-3.

Unadjusted Analysis for Pulmonary Questionnaire Variables by Group

Variable	Statistic	Group		Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison		
Asthma	n	995	1,298		
	Number/%				
	Yes	58 5.8%	62 4.8%	1.23 (0.85,1.78)	0.304
	No	937 94.2%	1,236 95.2%		
Bronchitis	n	994	1,298		
	Number/%				
	Yes	187 18.8%	240 18.5%	1.02 (0.83,1.26)	0.886
	No	807 81.2%	1,058 81.5%		
Pleurisy	n	993	1,296		
	Number/%				
	Yes	60 6.0%	7 5.9%	1.03 (0.73,1.46)	0.926
	No	933 94.0%	1,220 94.1%		
Pneumonia	n	995	1,298		
	Number/%				
	Yes	220 22.1%	321 24.7%	0.86 (0.71,1.05)	0.157
	No	775 77.9%	977 75.3%		
Tuberculosis	n	995	1,298		
	Number/%				
	Yes	9 0.9%	8 0.6%	1.47 (0.57,3.83)	0.578
	No	986 99.1%	1,290 99.4%		

TABLE 20-4.

Adjusted Analysis for Pulmonary Questionnaire Variables by Group

Variable	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
Asthma	n	995	1,298	1.29 (0.89,1.87)	0.178	OCC*CSMOK (p=0.007)
Bronchitis	n	994	1,298	1.01 (0.82,1.25)	0.898	RACE*PACKYR (p=0.005)
Pleurisy	n	993	1,296	1.02 (0.72,1.44)	0.932	PACKYR (p=0.005)
Pneumonia	n	995	1,298	****	****	GRP*PACKYR (p=0.004) AGE (p<0.001) OCC*PACKYR (p=0.033)

GRP: Group (Ranch Hand, Comparison).

****Group-by-covariate interaction (p<0.01)--adjusted relative risk, confidence interval, and p-value not presented.

contains the dependent variable-covariate associations. The summary of the group-by-covariate interactions for the group contrasts on the pulmonary variables can be found in Table Q-2 of Appendix Q.

Asthma

As shown in Table 20-3, no difference between the Ranch Hands and Comparisons was detected in the unadjusted analysis of asthma ($p=0.304$).

Based on pooled group data, none of the covariate tests of association with asthma were significant.

In the adjusted analysis of asthma, there was no significant difference between the two groups ($p=0.178$). In the adjusted model, the occupation-by-current cigarette smoking interaction was significant ($p=0.007$).

Bronchitis

No significant group difference was identified in the unadjusted analysis of bronchitis ($p=0.886$).

The covariate tests of association showed that race, current cigarette smoking, and lifetime cigarette smoking history were statistically significant ($p=0.002$, $p=0.009$, and $p=0.042$, respectively). A higher percentage of non-blacks reported having had bronchitis than Blacks (19.3% vs. 8.8%). For current cigarette smoking, 22.2 percent of the heavy smokers and 20.6 percent of the former smokers reported having experienced bronchitis in the past, as contrasted to 15.8 percent of the nonsmokers and 15.4 percent of the moderate smokers. For lifetime cigarette smoking history, the percentage of reported bronchitis increased with the frequency of smoking (15.7% for nonsmokers, 18.2% for moderate smokers, and 20.7% for heavy smokers).

The adjusted analysis of bronchitis also did not detect a significant difference between the Ranch Hands and the Comparisons ($p=0.898$). The race-by-lifetime cigarette smoking history interaction was significant ($p=0.005$).

Pleurisy

The results of the unadjusted analysis of pleurisy did not detect a significant group difference ($p=0.926$).

Based on pooled group data, the covariate associations with pleurisy showed that age, current cigarette smoking, and lifetime cigarette smoking history were borderline significant ($p=0.091$, $p=0.052$, and $p=0.055$, respectively). The rate of pleurisy increased with age (5.1% for those born in or after 1942, 6.3% for those born between 1923 and 1941, and 10.7% for those born in or before 1922). For current cigarette smoking, 4.5 percent of the nonsmokers, 7.0 percent of the former smokers, 4.4 percent of the moderate smokers, and 7.6 percent of the heavy smokers responded yes to having experienced pleurisy. Based on lifetime cigarette smoking history, the rates of pleurisy were 4.5, 5.4, and 7.2 percent for nonsmokers, moderate smokers, and heavy smokers, respectively.

In the adjusted analysis, no significant difference between the two groups was detected ($p=0.932$). In the adjusted model, lifetime cigarette smoking history was significant ($p=0.005$).

Pneumonia

In the unadjusted analysis of pneumonia, no significant difference between the Ranch Hands and the Comparisons was found ($p=0.157$).

Four of the five covariate tests of association with pneumonia were significant: age ($p<0.001$), race ($p=0.020$), current cigarette smoking ($p=0.003$), and lifetime cigarette smoking history ($p=0.024$). The number of participants who reported having had pneumonia increased with age (18.4% for those born in or after 1942, 27.0% for those born between 1923 and 1941, and 32.1% for those born in or before 1922). The rate for nonblacks was higher than for Blacks (24.1% vs. 15.3%). Based on current cigarette smoking, 20.7 percent of the nonsmokers, 26.5 percent of the former smokers, 18.7 percent of the moderate smokers, and 26.6 percent of the heavy smokers reported yes to having had pneumonia. For lifetime cigarette smoking history, the rate of pneumonia was found to increase with smoking intensity (20.7% for nonsmokers, 22.3% for moderate smokers, and 26.2% for heavy smokers).

The results of the adjusted analysis of pneumonia showed a significant group-by-lifetime cigarette smoking history interaction ($p=0.004$). Age and occupation-by-lifetime cigarette smoking history were significant terms in the model ($p<0.001$ and $p=0.033$, respectively). As shown in Table Q-2 of Appendix Q, the Comparisons in the heavy smoking category had a significantly higher reported history of pneumonia than the Ranch Hands (29.6% vs. 21.9%; Adj. RR: 0.66, 95% C.I.: [0.50, 0.88], $p=0.005$). No significant differences were detected between the Ranch Hands and the Comparisons in the nonsmoking and moderate smoking strata ($p=0.690$ and $p=0.266$, respectively).

Tuberculosis

The unadjusted analysis of tuberculosis did not detect a significant difference between the Ranch Hands and the Comparisons ($p=0.578$). Only nine Ranch Hands and eight Comparisons reported having had tuberculosis. Due to the low frequency of occurrence, an adjusted analysis was not conducted.

Physical Examination Variables

The unadjusted and adjusted results of the physical examination variables are presented in Tables 20-5 and 20-6, respectively. The dependent variable-covariate associations and group-by-covariate interactions are provided in Appendix Q in Tables Q-1 and Q-2, respectively.

Thorax and Lung Abnormalities

The unadjusted analysis of thorax and lung abnormalities showed a significant difference between the Ranch Hands and the Comparisons (Est. RR:

TABLE 20-5.

Unadjusted Analysis for Pulmonary Physical Examination Variables by Group

Variable	Statistic	Group				Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand		Comparison			
Thorax and Lung Abnormalities	n	995		1,299			
	Number/%						
	Yes	74	7.4%	65	5.0%	1.53 (1.08,2.15)	0.020
No	921	92.6%	1,234	95.0%			
Asymmetric Expansion	n	995		1,299			
	Number/%						
	Yes	0	0.0%	1	0.1%	-- ^a	0.999
No	995	100.0%	1,298	99.9%			
Hyperresonance	n	995		1,299			
	Number/%						
	Yes	40	4.0%	35	2.7%	1.51 (0.96,2.40)	0.100
No	955	96.0%	1,264	97.3%			
Dullness	n	995		1,299			
	Number/%						
	Yes	2	0.2%	1	0.1%	2.61 (0.24,28.87)	0.802
No	993	99.8%	1,298	99.9%			
Wheezes	n	995		1,299			
	Number/%						
	Yes	30	3.0%	25	1.9%	1.58 (0.93,2.71)	0.121
No	965	97.0%	1,274	98.1%			

TABLE 20-5. (continued)

Unadjusted Analysis for Pulmonary Physical Examination Variables by Group

Variable	Statistic	Group		Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison		
Rales	n	995	1,299		
	Number/%				
	Yes	14 1.4%	16 1.2%	1.14 (0.56,2.36)	0.850
	No	981 98.6%	1,283 98.8%		
X-Ray Interpretation	n	991	1,295		
	Number/%				
	Abnormal	48 4.8%	71 5.5%	0.88 (0.60,1.28)	0.560
	Normal	943 95.2%	1,224 94.5%		

--*Relative risk/confidence interval not given due to a cell with zero frequency.

TABLE 20-6.

Adjusted Analysis for Pulmonary Physical Examination Variables by Group

Variable	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
Thorax and Lung Abnormalities	n	995	1,299	1.39 (0.97,2.00)	0.072	AGE (p<0.001) OCC (p<0.001) CSMOK (p<0.001) PACKYR (p=0.030)
Hyper-resonance	n	995	1,299	1.36 (0.84,2.20)**	0.208**	GRP*OCC (p=0.017) AGE (p<0.001) CSMOK (p<0.001)
Wheezes	n	995	1,299	1.37 (0.79,2.38)	0.267	AGE (p=0.004) PACKYR (p=0.035) CSMOK (p<0.001)
Rales	n	995	1,299	1.05 (0.50,2.21)	0.895	AGE (p<0.001) CSMOK (p=0.001)
X-Ray Interpretation	n	991	1,295	0.84 (0.57,1.23)**	0.367**	GRP*RACE (p=0.023) AGE (p<0.001) CSMOK (p=0.002)

**Group-by-covariate interaction ($0.01 < p \leq 0.05$)--relative risk and p-value derived from a model fitted after deletion of this interaction.

1.53, 95% C.I.: [1.08,2.15], $p=0.020$). Among the Ranch Hands, 7.4 percent had abnormalities, as contrasted with 5.0 percent in the Comparisons.

Based on pooled group data, the covariate tests of association with thorax and lung abnormalities were significant for age, occupation, current cigarette smoking, and lifetime cigarette smoking history ($p<0.001$ for all). The association between thorax and lung abnormalities and race was borderline significant ($p=0.055$). The percentage of thorax and lungs abnormalities was found to increase with age (2.2% for those born in or after 1942, 8.5% for those born between 1923 and 1941, and 14.3% for those born in or before 1922). A higher percentage of abnormalities was detected in nonblacks than Blacks (6.3% vs. 2.2%). Enlisted flyers had the highest percentage of thorax and lung abnormalities (11.2% for enlisted flyers vs. 4.1% for officers and 5.8% for enlisted groundcrew). The prevalence rate was found to be increasing with the level of smoking, based on both current and lifetime cigarette smoking patterns. For current cigarette smoking, there were 1.3 percent abnormalities for nonsmokers, 5.1 percent for former smokers, 10.3 percent for moderate smokers, and 12.2 percent for heavy smokers. Based on lifetime cigarette smoking history, the percentages of participants with thorax and lung abnormalities were 1.3, 4.6, and 9.9 for nonsmokers, moderate smokers, and heavy smokers, respectively.

The result of the adjusted analysis on thorax and lung abnormalities was borderline significant (Adj. RR: 1.39, 95% C.I.: [0.97,2.00], $p=0.072$). Age, occupation, current cigarette smoking, and lifetime cigarette smoking history were significant covariates in the adjusted model ($p<0.001$, $p<0.001$, $p<0.001$, and $p=0.030$, respectively). The change from significance in the unadjusted analysis to borderline significance in the adjusted analysis is probably due to the association of thorax and lung abnormalities with current cigarette smoking, in conjunction with the association of group status and this smoking variable, as shown in Chapter 2.

Asymmetric Expansion

No difference between the two groups was detected in the unadjusted analysis of asymmetric expansion ($p=0.999$). Among all of the participants, there was only one occurrence of asymmetric expansion, which was in the Comparison group. An adjusted analysis was not conducted due to the sparse occurrence of this condition.

Hyperresonance

Based on the unadjusted analysis, the difference between the two groups on hyperresonance was borderline significant (Est. RR: 1.51, 95% C.I.: [0.96, 2.40], $p=0.100$). The percentages of participants with hyperresonance in the Ranch Hands and the Comparisons were 4.0 and 2.7, respectively.

The significant covariate associations with hyperresonance were age ($p<0.001$), occupation ($p=0.003$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). The prevalence rate increased with age (0.9% for those born in or after 1942, 4.5% for those born between 1923 and 1941, and 11.9% for those born in or before 1922). Hyperresonance

was found to be highest for enlisted flyers (6.0% for enlisted flyers versus 2.3% for officers and 3.1% for enlisted groundcrew). For both current cigarette smoking and lifetime cigarette smoking history, the prevalence rates of hyperresonance increased with smoking intensity. Based on current cigarette smoking, 1.0 percent of the nonsmokers were diagnosed with hyperresonance, as contrasted with 2.3 percent of the former smokers, 5.6 percent of the moderate smokers, and 7.0 percent of the heavy smokers. The rates were 1.0, 1.7, and 5.6 for nonsmokers, moderate smokers, and heavy smokers, respectively, based on lifetime cigarette smoking history.

In the adjusted analysis of hyperresonance, there was a significant group-by-occupation interaction ($p=0.017$). Age and current cigarette smoking were significant covariates ($p<0.001$ for both). Stratifying by occupation, a significant difference was detected between the two groups for the enlisted flyers (Adj. RR: 3.97, 95% C.I.: [1.48, 10.64], $p=0.006$). The Ranch Hand enlisted flyers had a significantly higher prevalence rate than the Comparison enlisted flyers (9.9% vs. 2.8%). No differences were identified in the officer and enlisted groundcrew occupational categories ($p=0.302$ and $p=0.746$, respectively). Without the group-by-occupation interaction in the model, no significant difference between the two groups was detected ($p=0.208$).

Dullness

Three participants, two Ranch Hands and one Comparison, were diagnosed with dullness of the lungs at the physical examination of the 1987 followup. No significant difference was detected in the unadjusted analysis ($p=0.802$). An adjusted analysis was not performed due to the low occurrence of dullness.

Wheezes

Based on the unadjusted analysis of wheezes, no difference was detected between the two groups ($p=0.121$).

The results of the covariate associations did not detect a significant association for race; however, there were significant associations for age ($p=0.004$), occupation ($p=0.010$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). The prevalence rate for wheezes increased with age (1.1% for those born in or after 1942, 3.3% for those born between 1923 and 1941, and 3.6% for those born in or before 1922). The rate in the enlisted flyers was 4.4 percent, as contrasted to 1.6 percent in the officers and 2.3 percent in the enlisted groundcrew. Based on current cigarette smoking, the nonsmokers had the lowest rate of wheezes, 0.3 percent, followed by 1.4 percent for the former smokers, 3.9 percent for the moderate smokers, and 6.8 percent for heavy smokers. For lifetime cigarette smoking, the prevalence rates for the nonsmokers, moderate smokers, and heavy smokers were 0.3 percent, 2.2 percent, and 3.8 percent, respectively.

In the adjusted analysis of wheezes, no significant difference between groups was detected ($p=0.267$). Age ($p=0.004$), lifetime cigarette smoking ($p=0.035$), and current cigarette smoking ($p<0.001$) were significant covariates.

Rales

No significant difference between the Ranch Hands and the Comparisons was identified in the unadjusted analysis of rales ($p=0.850$).

The covariate tests of association with rales revealed that age ($p<0.001$), occupation ($p=0.048$), current cigarette smoking ($p=0.009$), and lifetime cigarette smoking history ($p<0.001$) were significant. The prevalence rate of rales increased with age: 0.1 percent of the participants born in or after 1942 were diagnosed with rales, as contrasted to 1.9 percent of those born between 1923 and 1941 and 6.0 percent of those born in or before 1922. The highest rate was in the enlisted flyer occupational category (2.6% for enlisted flyers vs. 1.0% for officers and 1.1% for enlisted groundcrew). For current cigarette smoking, the highest percentage of rales was in the moderate smokers (2.6%), followed by the former smokers (1.5%), the heavy smokers (1.4%), and the nonsmokers (0.2%). Based on lifetime cigarette smoking history, the prevalence rate increased with the level of smoking (0.2% for nonsmokers, 0.5% for moderate smokers, and 2.5% for heavy smokers).

In the adjusted analysis of rales, no significant group difference was detected ($p=0.895$). Age and current cigarette smoking were significant covariates in the adjusted model ($p<0.001$ and $p=0.001$, respectively).

X-Ray Interpretation

Based on the unadjusted analysis, no significant difference between the two groups was detected in the unadjusted analysis of chest x-ray interpretation ($p=0.560$).

Using combined Ranch Hand and Comparison data, the covariate tests detected significant associations between x-ray abnormalities and age ($p<0.001$), occupation ($p=0.020$), current cigarette smoking ($p=0.006$), and lifetime cigarette smoking history ($p=0.003$). The association between x-ray abnormalities and race was borderline significant ($p=0.098$). The percentage of x-ray abnormalities increased with age. Only 3.0 percent of the participants born in or after 1942 had x-ray abnormalities, as contrasted to 6.6 percent of those born between 1923 and 1941 and 9.5 percent of those born in or before 1922. Blacks had a marginally higher percentage of abnormalities than nonblacks (8.8% vs. 5.0%). The highest percentage of abnormalities was in the enlisted flyers (8.1% for enlisted flyers vs. 4.6% for officers and 4.7% for enlisted groundcrew). Based on current cigarette smoking patterns, the moderate and heavy smokers had the highest percentages of abnormalities (8.0% and 6.0%, respectively). The current nonsmokers and former smokers had 3.0 percent and 5.2 percent abnormalities, respectively. For lifetime cigarette smoking history, the percentage of abnormalities increased with the level of smoking (2.9% for nonsmokers, 4.9% for moderate smokers, and 6.5% for heavy smokers).

In the adjusted analysis of chest x-ray interpretation, there was a significant group-by-race interaction ($p=0.023$). Age and current cigarette smoking were significant covariates in the model ($p<0.001$ and $p=0.002$, respectively). After stratifying by race, it was determined that there were more x-ray abnormalities among the Black Ranch Hands than the Black

Comparisons (14.0% vs. 5.0%); this result was borderline significant (Adj. RR: 3.27, 95% C.I.: [0.91, 11.68], $p=0.068$). No difference between the nonblack Ranch Hands and Comparisons was detected ($p=0.119$). The adjusted analysis without the group-by-race interaction did not reveal a significant difference ($p=0.367$).

Laboratory Examination Variables

Tables 20-7 and 20-8 contain the results of the unadjusted and adjusted analyses of the physiology laboratory variables for the pulmonary assessment. Covariate associations and group-by-covariate interactions are presented in Tables Q-1 and Q-2 of Appendix Q, respectively.

Technical quality of the pulmonary function testing was a major focus of quality control during the physical examination. The primary factors in achieving technical quality are the skill of the technician, the equipment, and the ability of the participants to give reproducible patterns over two or three runs. For each participant, technical quality was recorded as adequate or inadequate; measurements for two Ranch Hands were missing. The technical quality for seven Ranch Hands and two Comparisons was classified as inadequate (0.7% for Ranch Hands and 0.2% for Comparisons). The combined percentage was judged to be very low. The difference in technical quality between the Ranch Hands and Comparisons was marginally significant ($p=0.075$), although the technician was blind to the group membership of the participants and the same procedures and equipment were used throughout the 1987 followup.

FVC

No difference was found between the Ranch Hands and the Comparisons based on the unadjusted analysis of FVC ($p=0.368$).

Using the pooled Ranch Hand and Comparison data, the covariate tests with FVC showed significant associations for all five covariates: age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history ($p<0.001$ for all). The analysis showed that FVC was negatively correlated with age ($r=-0.094$). The mean FVC for Blacks was significantly lower than for nonblacks (85.7% vs. 97.5%). The lowest mean FVC was observed in the enlisted groundcrew occupational category (95.6%). The mean FVC for the officers and the enlisted flyers was 98.6 percent and 96.0 percent, respectively. FVC was negatively correlated with both current cigarette smoking and lifetime cigarette smoking history ($r=-0.139$ and $r=-0.200$, respectively).

The adjusted analysis of FVC did not detect a significant difference between the two groups ($p=0.580$). Race ($p<0.001$), occupation ($p<0.001$), lifetime cigarette smoking history ($p<0.001$), and an age-by-current cigarette smoking interaction ($p=0.049$) were significant terms in the adjusted model.

FEV₁

Based on the unadjusted analysis of FEV₁, no group difference was detected ($p=0.329$).

TABLE 20-7.

Unadjusted Analysis for Pulmonary Laboratory Examination Variables by Group

Variable	Statistic	Group		Contrast	Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison			
FVC	n	993	1,299			
	Mean	96.5	97.0		--	0.368
	95% C.I.	(95.7,97.3)	(96.3,97.7)			
FEV ₁	n	993	1,299			
	Mean	97.3	97.9		--	0.329
	95% C.I.	(96.3,98.3)	(97.1,98.8)			
FEV ₂	n	993	1,299			
	Mean	95.4	96.0		--	0.330
	95% C.I.	(94.5,96.3)	(95.2,96.8)			
FEV ₃	n	993	1,299			
	Mean	95.3	95.9		--	0.336
	95% C.I.	(94.5,96.2)	(95.1,96.7)			
FEFmax	n	993	1,299			
	Mean	136.6	137.5		--	0.344
	95% C.I.	(135.0,138.1)	(136.2,138.8)			
Ratio of Observed FEV ₁ to Observed FVC	n	993	1,299			
	Mean ^a	0.813	0.814		--	0.816
	95% C.I. ^a	(0.809,0.818)	(0.811,0.818)			

TABLE 20-7. (continued)

Unadjusted Analysis for Pulmonary Laboratory Examination Variables by Group

Variable	Statistic	Group		Comparison	Contrast	Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand					
Loss of Vital Capacity	n	993		1,299			
	Number/%						
	None	887 89.3%		1,173 90.3%	Overall		0.670
	Mild	85 8.6%		104 8.0%	Mild vs. None	1.08 (0.80,1.46)	0.664
	Mod./Sev.	21 2.1%		22 1.7%	Mod./Sev. vs. None	1.26 (0.69,2.31)	0.544
Obstructive Abnormality	n	993		1,299			
	Number/%						
	None	691 69.6%		942 72.5%	Overall		0.299
	Mild	255 25.7%		299 23.0%	Mild vs. None	1.16 (0.96,1.41)	0.140
	Mod./Sev.	47 4.7%		58 4.5%	Mod./Sev. vs. None	1.11 (0.74,1.64)	0.694

--Estimated relative risk not applicable for continuous analysis of a variable.

*Transformed from natural logarithm (1-X) scale.

TABLE 20-8.

Adjusted Analysis for Pulmonary Laboratory Examination Variables by Group

Variable	Statistic	Group		Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison				
FVC	n Adj. Mean 95% C.I.	993 91.4 (90.1,92.7)	1,299 91.7 (90.5,92.9)		—	0.580	RACE (p<0.001) OCC (p<0.001) PACKYR (p<0.001) AGE*CSMOK (p=0.049)
FEV ₁	n Adj. Mean** 95% C.I.**	993 92.9 (91.5,94.4)	1,299 93.2 (91.7,94.6)		—	0.721**	GRP*AGE (p=0.037) RACE (p<0.001) OCC (p=0.005) AGE*CSMOK (p=0.001) CSMOK*PACKYR (p<0.001)
FEV ₂	n Adj. Mean** 95% C.I.**	993 90.7 (89.3,92.0)	1,299 90.9 (89.6,92.2)		—	0.652**	GRP*AGE (p=0.042) RACE (p<0.001) OCC (p<0.001) AGE*CSMOK (p<0.001) CSMOK*PACKYR (p=0.002)
FEV ₃	n Adj. Mean 95% C.I.	993 90.4 (89.1,91.7)	1,299 90.6 (89.4,91.9)		—	0.621	RACE (p<0.001) OCC (p<0.001) AGE*CSMOK (p=0.001) CSMOK*PACKYR (p=0.006)
FEF _{max}	n Adj. Mean 95% C.I.	993 137.4 (135.9,138.9)	1,299 137.7 (136.4,139.0)		—	0.778	AGE*PACKYR (p=0.008) OCC*PACKYR (p=0.027) CSMOK*PACKYR (p=0.006)

TABLE 20-8. (continued)

Adjusted Analysis for Pulmonary Laboratory Examination Variables by Group

Variable	Statistic	Group		Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison				
Ratio of Observed FEV ₁ to Observed FVC	n Adj. Mean ^a 95% C.I. ^a	993 0.818 (0.811,0.825)	1,299 0.817 (0.810,0.824)		—	0.645	AGE*OCC (p=0.013) RACE*PACKYR (p=0.047) CSMOK*PACKYR (p=0.001)
Loss of Vital Capacity	n	993	1,299	Overall		0.679	AGE (p<0.001)
				Mild vs. None	1.08 (0.80,1.46)	0.623	RACE (p<0.001)
				Mod./Sev. vs. None	1.26 (0.70,2.27)	0.445	PACKYR (p<0.001)
Obstructive Abnormality	n	993	1,299	Overall		0.389	AGE (p<0.001)
				Mild vs. None	1.15 (0.94,1.42)	0.175	OCC (p=0.011)
				Mod./Sev. vs. None	1.11 (0.74,1.65)	0.610	PACKYR (p<0.001)

—Adjusted relative risk not applicable for continuous analysis of a variable.

**Group-by-covariate interaction ($0.01 < p < 0.05$)—adjusted mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

^aTransformed from natural logarithm (1-X) scale.

The covariate tests for FEV_1 revealed significant relationships with all five covariates ($p < 0.001$ for age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history). The analysis identified a negative correlation between FEV_1 and age ($r = -0.170$). The Blacks had a lower mean FEV_1 than nonblacks (89.1% vs. 98.2%). The lowest mean FEV_1 was observed in the enlisted flyers (95.1%) followed by the enlisted groundcrew (97.1%) and officers (99.4%). The analysis showed negative correlations for current cigarette smoking and lifetime cigarette smoking history ($r = -0.230$ and $r = -0.298$, respectively).

In the adjusted analysis of FEV_1 , there was a significant group-by-age interaction ($p = 0.037$). Race ($p < 0.001$), occupation ($p = 0.005$), an age-by-current cigarette smoking interaction ($p = 0.001$), and a current cigarette smoking-by-lifetime cigarette smoking history interaction ($p < 0.001$) were also significant terms in the model. As shown in Table Q-2 of Appendix Q, stratifying by age showed a significant difference between the two groups for those who were born between 1923 and 1941 ($p = 0.022$) and a borderline significant difference for those born in or before 1922 ($p = 0.081$). The adjusted mean of the Ranch Hands was significantly lower than the adjusted mean of the Comparisons for those born between 1923 and 1941 (90.0% vs. 91.9%); however, for those born in or before 1922, the adjusted mean of the Comparisons was marginally lower than the adjusted mean of the Ranch Hands (86.8% vs. 92.4%). No difference between the two groups was shown for those born in or after 1942 ($p = 0.126$). Without the group-by-age interaction in the model, no difference between the two groups was detected ($p = 0.721$).

FEV_2

The results of the unadjusted analysis of FEV_2 showed no significant difference between the two groups ($p = 0.330$).

Based on pooled group data, all covariate tests of association with FEV_2 were found to be statistically significant ($p < 0.001$ for age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history). FEV_2 was negatively correlated with age, current cigarette smoking, and lifetime cigarette smoking history ($r = -0.140$, $r = -0.204$, and $r = -0.271$, respectively). The means of the Blacks and nonblacks were 85.9 percent and 96.4 percent, respectively. The lowest FEV_2 was found in the enlisted flyers (93.8% for enlisted flyers vs. 94.9% in the enlisted groundcrew and 97.6% in the officers).

In the adjusted analysis, there was a significant group-by-age interaction ($p = 0.042$). The other significant effects in the model were race ($p < 0.001$), occupation ($p < 0.001$), age-by-current cigarette smoking interaction ($p < 0.001$), and current cigarette smoking-by-lifetime cigarette smoking history interaction ($p = 0.002$). Stratification by age revealed a significant difference between the two groups for those born between 1923 and 1941 (88.1% for Ranch Hands vs. 90.0% for Comparisons; $p = 0.017$) and a borderline significant difference for those born in or before 1922 (91.1% for Ranch Hands vs. 85.7% for Comparisons; $p = 0.070$). No difference was identified between the Ranch Hands and the Comparisons based on the adjusted analysis of FEV_2 without the group-by-age interaction ($p = 0.652$).

FEV₃

No difference between the Ranch Hand and Comparison groups was detected in the unadjusted analysis of FEV₃ (p=0.336).

The covariate tests with FEV₃ were significant for age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history (p<0.001 for all). There was a negative correlation between FEV₃ and age (r=-0.145). The mean FEV₃ was lower for Blacks than nonblacks (85.3% vs. 96.3%). The results for occupation showed that the lowest mean level was in the enlisted flyer occupation category (94.0% for enlisted flyers, 94.8% for enlisted groundcrew, and 97.4% for officers). Current cigarette smoking and lifetime cigarette smoking were both negatively correlated with FEV₃ (r=-0.183 and r=-0.255, respectively).

Based on the adjusted analysis of FEV₃, no group difference was identified (p=0.621). Race (p<0.001), occupation (p<0.001), age-by-current cigarette smoking interaction (p=0.001), and current cigarette smoking-by-lifetime cigarette smoking history interaction (p=0.006) were significant terms in the adjusted model.

FEFmax

No group difference was revealed in the unadjusted analysis of FEFmax (p=0.344).

The results of the covariate tests with FEFmax showed significant associations for age, occupation, current cigarette smoking, and lifetime cigarette smoking history (p<0.001 for all). Negative correlations were found for age, current cigarette smoking, and lifetime cigarette smoking history (r=-0.077, r=-0.239, and r=-0.216, respectively). The mean FEFmax for officers, enlisted flyers, and enlisted groundcrew was 140.8 percent, 135.3 percent, and 134.7 percent, respectively.

The Ranch Hands and the Comparisons were not significantly different based on the adjusted analysis of FEFmax (p=0.778). There were three significant interactions involving lifetime cigarette smoking history in the model: age (p=0.008), occupation (p=0.027), and current smoking (p=0.006).

Ratio of Observed FEV₁ to Observed FVC

The unadjusted analysis of the ratio of observed FEV₁ to observed FVC did not identify a significant difference between the two groups (p=0.816).

The covariate tests with the ratio of observed FEV₁ to observed FVC showed significant associations for all five covariates: age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history (p<0.001 for all). Based on the positive correlation between age and 1 minus the ratio (r=0.263), the ratio was found to decrease as age increased. The mean of the nonblacks was 0.812, as contrasted to a mean of 0.841 for Blacks. The mean of the ratio of observed FEV₁ to observed FVC was 0.808 for officers, 0.800 for enlisted flyers, and 0.823 for enlisted groundcrew. The ratio also

decreased as current cigarette smoking and lifetime cigarette smoking increased, as demonstrated by the positive correlations with 1 minus the ratio ($r=0.190$ and $r=0.260$, respectively).

The Ranch Hands and the Comparisons did not differ significantly on the ratio of observed FEV₁ to observed FVC in the adjusted analysis ($p=0.645$). The significant terms of the model were: age-by-occupation interaction ($p=0.013$), race-by-lifetime cigarette smoking history interaction ($p=0.047$), and current cigarette smoking-by-lifetime cigarette smoking history interaction ($p=0.001$).

Loss of Vital Capacity

The unadjusted analysis of loss of vital capacity was not significant ($p=0.670$), nor were the contrasts of mild versus none and of moderate/severe versus none ($p=0.664$ and $p=0.544$, respectively).

The results of the covariate tests of association with loss of vital capacity showed that age ($p<0.001$), race ($p<0.001$), current cigarette smoking ($p=0.001$), and lifetime cigarette smoking history ($p<0.001$) were significant. For each level of loss of vital capacity (none, mild, and moderate/severe), the percentage of the participants in each category of the covariate is provided in Table Q-1 of Appendix Q.

In general, the loss of vital capacity increased with age. Of the participants born in or after 1942, 93.0 percent had no loss of vital capacity, as compared to 87.7 percent for those born between 1923 and 1941 and 86.9 percent for those born in or before 1922. Mild losses of vital capacity were detected in 6.3 percent of those born in or after 1942, 9.8 percent of those born between 1923 and 1941, and 8.3 percent of those born in or before 1922. The percentage of participants with a moderate/severe loss of vital capacity increased with age (0.7% for those born in or after 1942, 2.6% for those born between 1923 and 1941, and 4.8% for those born in or before 1922).

Blacks had a higher percentage of abnormalities than nonblacks. The percentage of participants with no loss of vital capacity was lower for Blacks than nonblacks (69.3% vs. 91.2%). Of the Black participants, 24.1 percent had a mild loss of vital capacity, as compared to 7.2 percent for nonblacks. Moderate/severe losses were detected in 6.6 percent of the Blacks and 1.6 percent of the nonblacks.

For current cigarette smoking, the loss of vital capacity increased with smoking intensity. For current cigarette smoking, 93.6 percent of the nonsmokers had no loss of vital capacity, as compared to 90.3 percent of the former smokers, 86.4 percent of the moderate smokers, and 86.2 percent of the heavy smokers. Mild losses were detected in 5.6 percent of the nonsmokers, 7.9 percent of the former smokers, 10.8 percent of the moderate smokers, and 10.8 percent of the heavy smokers based on current cigarette smoking habits. Only 0.8 percent of the nonsmokers had a moderate/severe loss of vital capacity, as compared with 1.8 percent for former smokers, 2.8 percent for moderate smokers, and 3.0 percent for heavy smokers using current cigarette smoking.

The loss of vital capacity also increased with lifetime smoking intensity. Based on this covariate, 93.6 percent of the nonsmokers had no loss of vital capacity, as contrasted with 92.1 percent of the moderate smokers and 86.2 percent of the heavy smokers. The percentage of participants with a mild loss was 5.6 percent for nonsmokers, 6.6 percent for moderate smokers, and 10.9 percent for heavy smokers. Moderate/severe losses were detected in 0.8 percent of the nonsmokers, 1.3 percent of the moderate smokers, and 2.9 percent of the heavy smokers.

The overall adjusted analysis of loss of vital capacity did not detect a difference between the two groups ($p=0.679$). Group differences were also not found in the adjusted analysis of the individual contrasts ($p=0.623$ for mild vs. none and $p=0.445$ for moderate/severe vs. none). Age, race, and lifetime cigarette smoking history were significant effects in the adjusted analysis ($p<0.001$ for all).

Obstructive Abnormality

In the unadjusted analysis of obstructive abnormality, no difference between the two groups was detected for the overall analysis of the three categories ($p=0.299$), or for either the mild versus none or the moderate/severe versus none contrasts ($p=0.140$ and $p=0.694$, respectively).

The covariate tests with obstructive abnormality showed that age, occupation, current cigarette smoking, and lifetime cigarette smoking history were significant ($p<0.001$ for all). Each participant was classified as having no obstructive abnormality, a mild obstructive abnormality, or a moderate/severe obstructive abnormality. For each level of obstructive abnormality, the percentage of participants by category of the covariate is provided in tabular form in Table Q-1 of Appendix Q.

The prevalence rate of obstructive abnormality increased with age. No obstructive abnormalities were detected in 84.4 percent of those born in or after 1942, 62.4 percent of those born between 1923 and 1941, and 52.4 percent of those born in or before 1922. Of those born in or before 1922, 38.1 percent had a mild obstructive abnormality, as compared to 30.7 percent of those born between 1923 and 1941 and 14.4 percent of those born in or after 1942. The same pattern of abnormalities was demonstrated for moderate/severe obstructive abnormalities (1.1% for those born in or after 1942, 6.9% for those born between 1923 and 1941, and 9.5% for those born in or before 1922).

The occupational category with the highest level of obstructive abnormalities was the enlisted flyers. No obstructive abnormalities were detected in 75.9 percent of the enlisted groundcrew, 70.6 percent of the officers, and 60.2 percent of the enlisted flyers. Of the enlisted flyers, 32.7 percent had a mild obstructive abnormality, as compared to 25.8 percent of the officers and 19.7 percent of the enlisted groundcrew. Moderate/severe obstructive abnormalities were detected in 7.1 percent of the enlisted flyers, 4.4 percent of the enlisted groundcrew, and 3.7 percent of the officers.

The percentage of obstructive abnormalities increased with levels of current cigarette smoking. Based on current cigarette smoking habits, 9.1 percent of the nonsmokers, 25.2 percent of the former smokers, 30.0 percent of the moderate smokers, and 41.2 percent of the heavy smokers had a mild

obstructive abnormality. The percentages of moderate/severe obstructive abnormalities were 1.0, 5.0, 5.4, and 8.9 for nonsmokers, former smokers, moderate smokers, and heavy smokers, respectively. No obstructive abnormalities were detected in 90.0 percent of the nonsmokers, 69.9 percent of the former smokers, 64.6 percent of the moderate smokers, and 49.9 percent of the heavy smokers.

The percentage of obstructive abnormalities was also found to increase based on lifetime cigarette smoking history. For lifetime cigarette smoking, 9.2 percent and 1.0 percent of the nonsmokers had mild and moderate/severe obstructive abnormalities, respectively, as contrasted with corresponding percentages of 21.5 and 4.1 for moderate smokers and 34.9 and 7.1 for heavy smokers. Only 58.0 percent of the heavy smokers had no obstructive abnormality, as compared to 74.4 percent of the moderate smokers and 89.8 percent of the nonsmokers.

The adjusted analysis of obstructive abnormality for the overall test, mild versus none, and moderate/severe versus none did not detect a difference between the Ranch Hands and the Comparisons ($p=0.389$, $p=0.175$, and $p=0.610$, respectively). The significant covariates were age ($p<0.001$), occupation ($p=0.011$), and lifetime cigarette smoking history ($p<0.001$).

Exposure Index Analysis

The results of the unadjusted and adjusted exposure index analyses are presented in Tables 20-9 and 20-10, respectively. A summary of the exposure index-by-covariate interactions is provided in Table 20-11; Table Q-3 of Appendix Q contains the detailed results of the interactions involving exposure index. The final interpretation of these exposure index data must await the reanalysis of the clinical data using the results of the serum dioxin assay. The report is expected in 1991.

Questionnaire Variables

Asthma

The results showed a significant difference in history of asthma for the overall test of officers ($p=0.045$) based on the unadjusted analysis and a borderline significant difference based on the adjusted analysis ($p=0.088$). Of the officers, 9.2 percent of the low exposure category reported having asthma, as contrasted with 3.2 percent of the officers in the medium and in the high exposure categories. All of the contrasts for the officers were borderline significant. Based on the unadjusted results, the estimated relative risk for both the medium versus low and high versus low contrasts was 0.33 (95% C.I.: [0.10,1.05] and $p=0.084$ for medium vs. low; 95% C.I.: [0.10,1.04] and $p=0.081$ for high vs. low). The adjusted relative risk from the adjusted analysis was 0.35 for both of the contrasts (95% C.I.: [0.11, 1.13] and $p=0.079$ for medium versus low; 95% C.I.: [0.11,1.14] and $p=0.082$ for high vs. low). Since the highest percentage of participants who reported having had asthma within the officer cohort was for the low exposure category, these results do not suggest a dose-response relationship.

The unadjusted and adjusted analyses for the enlisted flyers and enlisted groundcrew did not identify any significant results.

TABLE 20-9.

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Asthma	Officer	n	130		124		125		Overall		0.045
		Number/%									
		Yes	12	9.2%	4	3.2%	4	3.2%	M vs. L	0.33 (0.10,1.05)	0.084
		No	118	90.8%	120	96.8%	121	96.8%	H vs. L	0.33 (0.10,1.04)	0.081
	Enlisted Flyer	n	55		63		53		Overall		0.795
		Number/%									
		Yes	2	3.6%	4	6.3%	3	5.7%	M vs. L	1.80 (0.32,10.21)	0.812
		No	53	96.4%	59	93.7%	50	94.3%	H vs. L	1.59 (0.26,9.92)	0.964
	Enlisted Groundcrew	n	147		158		140		Overall		0.320
		Number/%									
		Yes	6	4.1%	13	8.2%	10	7.1%	M vs. L	2.11 (0.78,5.70)	0.206
		No	141	95.9%	145	91.8%	130	92.9%	H vs. L	1.81 (0.64,5.11)	0.384
Bronchitis	Officer	n	130		123		125		Overall		0.594
		Number/%									
		Yes	30	23.1%	22	17.9%	26	20.8%	M vs. L	0.73 (0.39,1.34)	0.386
		No	100	76.9%	101	82.1%	99	79.2%	H vs. L	0.88 (0.48,1.59)	0.774
	Enlisted Flyer	n	55		63		53		Overall		0.003
		Number/%									
		Yes	18	32.7%	5	7.9%	10	18.9%	M vs. L	0.18 (0.06,0.52)	0.001
		No	37	67.3%	58	92.1%	43	81.1%	H vs. L	0.48 (0.20,1.16)	0.154
	Enlisted Groundcrew	n	147		158		140		Overall		0.699
		Number/%									
		Yes	24	16.3%	25	15.8%	27	19.3%	M vs. L	0.96 (0.52,1.78)	0.999
		No	123	83.7%	133	84.2%	113	80.7%	H vs. L	1.23 (0.67,2.25)	0.616

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Pleurisy	Officer	n	130		124		124		Overall		0.142
		Number/%									
		Yes	8	6.2%	10	8.1%	3	2.4%	M vs. L	1.34 (0.51,3.51)	0.728
	Enlisted Flyer	No	122	93.9%	114	91.9%	121	97.6%	H vs. L	0.38 (0.10,1.46)	0.248
		n	55		63		53		Overall		0.807
		Number/%									
	Enlisted Groundcrew	Yes	3	5.5%	3	4.8%	4	7.5%	M vs. L	0.87 (0.17,4.48)	0.999
		No	52	94.5%	60	95.2%	49	92.5%	H vs. L	1.42 (0.30,6.65)	0.958
		n	146		158		140		Overall		0.356
	Pneumonia	Officer	Yes	13	8.9%	9	5.7%	7	5.0%	M vs. L	0.62 (0.26,1.49)
No			133	91.1%	149	94.3%	133	95.0%	H vs. L	0.54 (0.21,1.39)	0.288
n			130		124		125		Overall		0.628
Enlisted Flyer	Number/%										
	Yes	27	20.8%	25	20.2%	31	24.8%	M vs. L	0.96 (0.52,1.77)	0.999	
	No	103	79.2%	99	79.8%	94	75.2%	H vs. L	1.26 (0.70,2.26)	0.536	
Enlisted Groundcrew	n	55		63		53		Overall		0.439	
	Number/%										
	Yes	13	23.6%	14	22.2%	17	32.1%	M vs. L	0.92 (0.39,2.18)	0.999	
Enlisted Groundcrew	No	42	76.4%	49	77.8%	36	67.9%	H vs. L	1.53 (0.65,3.56)	0.446	
	n	147		158		140		Overall		0.503	
	Number/%										
Enlisted Groundcrew	Yes	35	23.8%	29	18.4%	29	20.7%	M vs. L	0.72 (0.41,1.25)	0.304	
	No	112	76.2%	129	81.6%	111	79.3%	H vs. L	0.84 (0.48,1.46)	0.626	

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value	
			Low		Medium		High					
Tubercu- losis	Officer	n	130		124		125		Overall		0.362	
		Number/%										
		Yes	1	0.8%	0	0.0%	2	1.6%	M vs. L	-- ^a	0.999	
		No	129	99.2%	124	100.0%	123	98.4%	H vs. L	2.10 (0.19,23.43)	0.970	
		Enlisted Flyer	n	55		63		53		Overall		0.105
			Number/%									
	Yes		0	0.0%	0	0.0%	2	3.8%	M vs. L	-- ^a	-- ^a	
		No	55	100.0%	63	100.0%	51	96.2%	H vs. L	-- ^a	0.476	
		Enlisted Groundcrew	n	147		158		140		Overall		0.206
			Number/%									
	Yes		0	0.0%	3	1.9%	1	0.7%	M vs. L	-- ^a	0.276	
		No	147	100.0%	155	98.1%	139	99.3%	H vs. L	-- ^a	0.976	
Thorax and Lung Abnormalities		n	130		124		125		Overall		0.235	
		Number/%										
	Yes	9	6.9%	7	5.6%	3	2.4%	M vs. L	0.80 (0.29,2.23)	0.874		
	No	121	93.1%	117	94.4%	122	97.6%	H vs. L	0.33 (0.09,1.25)	0.156		
	Enlisted Flyer	n	55		63		53		Overall		0.440	
		Number/%										
Yes		11	20.0%	9	14.3%	6	11.3%	M vs. L	0.67 (0.25,1.75)	0.562		
	No	44	80.0%	54	85.7%	47	88.7%	H vs. L	0.51 (0.17,1.50)	0.330		
	Enlisted Groundcrew	n	147		158		140		Overall		0.491	
		Number/%										
Yes		8	5.4%	9	5.7%	12	8.6%	M vs. L	1.05 (0.39,2.80)	0.999		
	No	139	94.6%	149	94.3%	128	91.4%	H vs. L	1.63 (0.65,4.11)	0.418		

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value	
			Low		Medium		High					
Asymmetric Expansion	Officer	n	130		124		125		Overall		-- ^a	
		Number/%										
		Yes	0	0.0%	0	0.0%	0	0.0%	M vs. L	-- ^a	-- ^a	
		No	130	100.0%	124	100.0%	125	100.0%	H vs. L	-- ^a	-- ^a	
		Enlisted Flyer	n	55		63		53		Overall		-- ^a
			Number/%									
	Yes		0	0.0%	0	0.0%	0	0.0%	M vs. L	-- ^a	-- ^a	
		No	55	100.0%	63	100.0%	53	100.0%	H vs. L	-- ^a	-- ^a	
		Enlisted Groundcrew	n	147		158		140		Overall		-- ^a
			Number/%									
	Yes		0	0.0%	0	0.0%	0	0.0%	M vs. L	-- ^a	-- ^a	
		No	147	100.0%	158	100.0%	140	100.0%	H vs. L	-- ^a	-- ^a	
Hyper-resonance		Officer	n	130		124		125		Overall		0.391
			Number/%									
	Yes		4	3.1%	2	1.6%	1	0.8%	M vs. L	0.52 (0.09,2.87)	0.728	
	No	126	96.9%	122	98.4%	124	99.2%	H vs. L	0.25 (0.03,2.31)	0.396		
	Enlisted Flyer	n	55		63		53		Overall		0.329	
		Number/%										
Yes		8	14.5%	4	6.3%	5	9.4%	M vs. L	0.40 (0.11,1.40)	0.244		
	No	47	85.5%	59	93.7%	48	90.6%	H vs. L	0.61 (0.19,2.01)	0.606		
	Enlisted Groundcrew	n	147		158		140		Overall		0.331	
		Number/%										
Yes		6	4.1%	3	1.9%	7	5.0%	M vs. L	0.46 (0.11,1.85)	0.432		
	No	141	95.9%	155	98.1%	133	95.0%	H vs. L	1.24 (0.41,3.78)	0.928		

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Dullness	Officer	n	130		124		125		Overall		-- ^a
		Number/%									
		Yes	0	0.0%	0	0.0%	0	0.0%	M vs. L	-- ^a	-- ^a
		No	130	100.0%	124	100.0%	125	100.0%	H vs. L	-- ^a	-- ^a
	Enlisted Flyer	n	55		63		53		Overall		0.422
		Number/%									
		Yes	0	0.0%	1	1.6%	0	0.0%	M vs. L	-- ^a	0.999
		No	55	100.0%	62	98.4%	53	100.0%	H vs. L	-- ^a	-- ^a
	Enlisted Groundcrew	n	147		158		140		Overall		0.362
		Number/%									
		Yes	1	0.7%	0	0.0%	0	0.0%	M vs. L	-- ^a	0.964
		No	146	99.3%	158	100.0%	140	100.0%	H vs. L	-- ^a	0.999
Wheezes	Officer	n	130		124		125		Overall		0.368
		Number/%									
		Yes	4	3.1%	4	3.2%	1	0.8%	M vs. L	1.05 (0.26,4.29)	0.999
		No	126	96.9%	120	96.8%	124	99.2%	H vs. L	0.25 (0.03,2.31)	0.396
	Enlisted Flyer	n	55		63		53		Overall		0.498
		Number/%									
		Yes	3	5.5%	4	6.3%	1	1.9%	M vs. L	1.18 (0.25,5.50)	0.999
		No	52	94.5%	59	93.7%	52	98.1%	H vs. L	0.33 (0.03,3.31)	0.646
	Enlisted Groundcrew	n	147		158		140		Overall		0.855
		Number/%									
		Yes	4	2.7%	4	2.5%	5	3.6%	M vs. L	0.93 (0.23,3.78)	0.999
		No	143	97.3%	154	97.5%	135	96.4%	H vs. L	1.32 (0.35,5.04)	0.940

TABLE 20-9. (continued)

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TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
FVC	Officer	n	129	124	125	Overall		0.647
		Mean	99.0	97.4	98.3	M vs. L	--	0.366
		95% C.I.	(96.4,101.6)	(95.1,99.8)	(96.1,100.6)	H vs. L	--	0.690
	Enlisted Flyer	n	54	63	53	Overall		0.241
		Mean	98.8	95.1	95.5	M vs. L	--	0.115
		95% C.I.	(95.1,102.5)	(92.4,97.9)	(92.0,99.0)	H vs. L	--	0.205
	Enlisted Groundcrew	n	147	158	140	Overall		0.629
		Mean	94.7	95.8	94.5	M vs. L	--	0.466
		95% C.I.	(92.7,96.7)	(93.6,98.0)	(92.4,96.5)	H vs. L	--	0.874
FEV ₁	Officer	n	129	124	125	Overall		0.340
		Mean	99.9	97.1	99.5	M vs. L	--	0.183
		95% C.I.	(96.8,103.1)	(94.5,99.8)	(96.9,102.1)	H vs. L	--	0.815
	Enlisted Flyer	n	54	63	53	Overall		0.832
		Mean	94.1	94.7	96.0	M vs. L	--	0.826
		95% C.I.	(89.0,99.1)	(91.1,98.4)	(91.8,100.1)	H vs. L	--	0.572
	Enlisted Groundcrew	n	147	158	140	Overall		0.174
		Mean	97.7	97.8	94.8	M vs. L	--	0.961
		95% C.I.	(95.3,100.2)	(95.3,100.4)	(92.2,97.3)	H vs. L	--	0.103

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
20-38 FEV ₂	Officer	n	129	124	125	Overall		0.453
		Mean	98.1	95.8	97.6	M vs. L	--	0.247
		95% C.I.	(95.2,101.0)	(93.4,98.3)	(95.2,99.9)	H vs. L	--	0.784
	Enlisted Flyer	n	54	63	53	Overall		0.974
		Mean	94.1	93.6	94.2	M vs. L	--	0.849
		95% C.I.	(89.9,98.4)	(90.4,96.8)	(90.3,98.0)	H vs. L	--	0.994
	Enlisted Groundcrew	n	147	158	140	Overall		0.339
		Mean	94.9	95.4	93.1	M vs. L	--	0.780
		95% C.I.	(92.7,97.1)	(93.0,97.8)	(90.8,95.3)	H vs. L	--	0.249
FEV ₃	Officer	n	129	124	125	Overall		0.540
		Mean	97.9	95.9	97.2	M vs. L	--	0.296
		95% C.I.	(95.0,100.7)	(93.5,98.3)	(95.0,99.5)	H vs. L	--	0.730
	Enlisted Flyer	n	54	63	53	Overall		0.863
		Mean	95.1	93.7	94.1	M vs. L	--	0.597
		95% C.I.	(91.1,99.0)	(90.7,96.8)	(90.4,97.8)	H vs. L	--	0.723
	Enlisted Groundcrew	n	147	158	140	Overall		0.427
		Mean	94.5	95.2	93.2	M vs. L	--	0.641
		95% C.I.	(92.3,96.6)	(92.9,97.5)	(91.0,95.3)	H vs. L	--	0.396

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
FEF _{max}	Officer	n	129	124	125	Overall		0.781
		Mean	141.2	140.1	142.3	M vs. L	--	0.724
		95% C.I.	(137.0, 145.4)	(135.6, 144.6)	(138.3, 146.3)	H vs. L	--	0.723
	Enlisted Flyer	n	54	63	53	Overall		0.134
		Mean	128.3	136.7	137.5	M vs. L	--	0.113
		95% C.I.	(120.2, 136.5)	(130.2, 143.2)	(131.7, 143.4)	H vs. L	--	0.076
	Enlisted Groundcrew	n	147	158	140	Overall		0.164
		Mean	136.1	133.5	130.7	M vs. L	--	0.325
		95% C.I.	(132.2, 140.0)	(129.9, 137.0)	(126.6, 134.9)	H vs. L	--	0.064
Ratio of Observed FEV ₁ to Observed FVC	Officer	n	129	124	125	Overall		0.226
		Mean ^b	0.810	0.799	0.812	M vs. L	--	0.176
		95% C.I. ^b	(0.799, 0.821)	(0.788, 0.810)	(0.801, 0.823)	H vs. L	--	0.780
	Enlisted Flyer	n	54	63	53	Overall		0.037
		Mean ^b	0.772	0.805	0.810	M vs. L	--	0.043
		95% C.I. ^b	(0.746, 0.796)	(0.784, 0.824)	(0.791, 0.827)	H vs. L	--	0.016
	Enlisted Groundcrew	n	147	158	140	Overall		0.047
		Mean ^b	0.831	0.828	0.813	M vs. L	--	0.654
		95% C.I. ^b	(0.822, 0.839)	(0.818, 0.837)	(0.801, 0.825)	H vs. L	--	0.020

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Loss of Vital Capacity	Officer	n	129		124		125		Overall		0.147
		Number/%									
		None	117	90.7%	110	88.7%	115	92.0%	M vs. L ^c	1.82 (0.69,4.80)	0.322
		Mild	7	5.4%	12	9.7%	10	8.0%	H vs. L ^c	1.45 (0.54,3.95)	0.628
		Mod./Sev.	5	3.9%	2	1.6%	0	0.0%	M vs. L ^d	0.43 (0.08,2.24)	0.520
								H vs. L ^d	-- ^a	0.069	
	Enlisted Flyer	n	54		63		53		Overall		0.582
		Number/%									
		None	50	92.6%	57	90.5%	48	90.6%	M vs. L ^c	1.75 (0.42,7.38)	0.678
		Mild	3	5.6%	6	9.5%	5	9.4%	H vs. L ^c	1.74 (0.39,7.67)	0.716
		Mod./Sev.	1	1.9%	0	0.0%	0	0.0%	M vs. L ^d	-- ^a	0.944
								H vs. L ^d	-- ^a	0.999	
	Enlisted Groundcrew	n	147		158		140		Overall		0.590
		Number/%									
		None	129	87.8%	138	87.3%	123	87.9%	M vs. L ^c	0.87 (0.39,1.92)	0.882
Mild		14	9.5%	13	8.2%	15	10.7%	H vs. L ^c	1.12 (0.52,2.43)	0.918	
Mod./Sev.		4	2.7%	7	4.4%	2	1.4%	M vs. L ^d	1.64 (0.47,5.72)	0.644	
							H vs. L ^d	0.52 (0.09,2.92)	0.744		

TABLE 20-9. (continued)

Unadjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Obstructive Abnormality	Officer	n	129		124		125		Overall		0.109
		Number/%									
		None	96	74.4%	76	61.3%	82	65.6%	M vs. L ^c	2.09 (1.18,3.70)	0.016
		Mild	26	20.2%	43	34.7%	39	31.2%	H vs. L ^c	1.76 (0.99,3.13)	0.075
		Mod./Sev.	7	5.4%	5	4.0%	4	3.2%	M vs. L ^d	0.90 (0.28,2.96)	0.999
								H vs. L ^d	0.67 (0.19,2.37)	0.760	
	Enlisted Flyer	n	54		63		53		Overall		0.265
		Number/%									
		None	25	46.3%	40	63.5%	34	64.2%	M vs. L ^c	0.46 (0.21,1.03)	0.089
		Mild	23	42.6%	17	27.0%	16	30.2%	H vs. L ^c	0.51 (0.23,1.16)	0.160
		Mod./Sev.	6	11.1%	6	9.5%	3	5.7%	M vs. L ^d	0.63 (0.18,2.15)	0.660
								H vs. L ^d	0.37 (0.08,1.61)	0.316	
	Enlisted Groundcrew	n	147		158		140		Overall		0.096
		Number/%									
		None	117	79.6%	126	79.4%	95	67.9%	M vs. L ^c	1.00 (0.55,1.80)	0.999
		Mild	26	17.7%	28	17.7%	37	26.4%	H vs. L ^c	1.75 (0.99,3.10)	0.072
		Mod./Sev.	4	2.7%	4	2.5%	8	5.7%	M vs. L ^d	0.93 (0.23,3.80)	0.999
								H vs. L ^d	2.46 (0.72,8.43)	0.238	

--^aEstimated relative risk/confidence interval/p-value not given due to cells with zero frequency.

--Estimated relative risk not applicable for continuous analysis of a variable.

^bTransformed from natural logarithm (1-X) scale.

^cMild contrasted with none.

^dModerate/severe contrasted with none.

TABLE 20-10.

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Asthma	Officer	n	130	124	125	Overall		0.088
						M vs. L	0.35 (0.11,1.13)	0.079
						H vs. L	0.35 (0.11,1.14)	0.082
	Enlisted Flyer	n	55	63	53	Overall		0.788
						M vs. L	1.85 (0.31,11.14)	0.501
						H vs. L	1.38 (0.21,8.85)	0.736
	Enlisted Groundcrew	n	147	158	140	Overall		0.326
						M vs. L	2.07 (0.75,5.71)	0.162
						H vs. L	1.82 (0.63,5.21)	0.267
Bronchitis	Officer	n	130	123	125	Overall		0.609
						M vs. L	0.73 (0.39,1.37)	0.327
						H vs. L	0.90 (0.49,1.65)	0.732
	Enlisted Flyer	n	55	63	53	Overall		0.003
						M vs. L	0.18 (0.06,0.53)	0.002
						H vs. L	0.47 (0.19,1.17)	0.104
	Enlisted Groundcrew	n	147	158	140	Overall		0.662
						M vs. L	0.89 (0.48,1.67)	0.716
						H vs. L	1.18 (0.64,2.20)	0.594

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Pleurisy	Officer	n	130	124	124	Overall		0.121
						M vs. L	1.20 (0.45,3.23)	0.714
						H vs. L	0.35 (0.09,1.37)	0.131
	Enlisted Flyer	n	55	63	53	Overall		0.822
						M vs. L	0.97 (0.18,5.10)	0.973
						H vs. L	1.52 (0.31,7.41)	0.601
	Enlisted Groundcrew	n	146	158	140	Overall		0.340**
						M vs. L	0.64 (0.26,1.58)**	0.338**
						H vs. L	0.50 (0.19,1.32)**	0.163**
Pneumonia	Officer	n	130	124	125	Overall		0.563**
						M vs. L	0.83 (0.44,1.56)**	0.567**
						H vs. L	1.16 (0.64,2.11)**	0.630**
	Enlisted Flyer	n	55	63	53	Overall		0.429**
						M vs. L	1.06 (0.44,2.59)**	0.893**
						H vs. L	1.70 (0.70,4.12)**	0.240**
	Enlisted Groundcrew	n	147	158	140	Overall		0.468
						M vs. L	0.72 (0.41,1.27)	0.256
						H vs. L	0.75 (0.42,1.34)	0.333

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Thorax and Lung Abnormalities	Officer	n	130	124	125	Overall		0.067
						M vs. L	0.73 (0.25,2.19)	0.578
						H vs. L	0.20 (0.04,0.93)	0.040
	Enlisted Flyer	n	55	63	53	Overall		0.725
						M vs. L	0.77 (0.27,2.19)	0.619
						H vs. L	0.63 (0.20,2.00)	0.434
	Enlisted Groundcrew	n	147	158	140	Overall		0.602
						M vs. L	1.55 (0.54,4.42)	0.417
						H vs. L	1.58 (0.59,4.26)	0.361
Hyper-resonance	Officer	n	130	124	125	Overall		0.139**
						M vs. L	0.33 (0.05,2.20)**	0.254**
						H vs. L	0.10 (0.01,1.60)**	0.104**
	Enlisted Flyer	n	55	63	53	Overall		0.530
						M vs. L	0.49 (0.13,1.93)	0.310
						H vs. L	0.96 (0.26,3.57)	0.956
	Enlisted Groundcrew	n	147	158	140	Overall		0.828**
						M vs. L	0.75 (0.17,3.35)**	0.707**
						H vs. L	1.17 (0.34,4.00)**	0.799**

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
20-45	Wheezes	Officer n	130	124	125	Overall		0.104
						M vs. L	0.93 (0.21,4.20)	0.928
						H vs. L	0.10 (0.01,1.71)	0.111
	Enlisted Flyer	n	55	63	53	Overall		0.613
						M vs. L	1.26 (0.25,6.40)	0.783
						H vs. L	0.44 (0.04,4.66)	0.492
	Enlisted Groundcrew	n	147	158	140	Overall		0.733**
						M vs. L	1.80 (0.37,8.74)**	0.467**
						H vs. L	1.58 (0.36,6.88)**	0.546**
	Rales	Officer n	130	124	125	Overall		0.237
						M vs. L	0.44 (0.04,5.15)	0.511
						H vs. L	— ^a	— ^a
	Enlisted Flyer	n	95	63	53	Overall		0.865
						M vs. L	0.71 (0.10,5.24)	0.734
						H vs. L	0.58 (0.08,4.40)	0.603
	Enlisted Groundcrew	n	147	158	140	Overall		0.979
						M vs. L	1.35 (0.06,29.41)	0.849
						H vs. L	1.27 (0.08,19.11)	0.865

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
X-Ray Interpretation	Officer	n	130	124	124	Overall		0.395
						M vs. L	0.51 (0.13,1.98)	0.329
						H vs. L	1.17 (0.38,3.61)	0.783
	Enlisted Flyer	n	55	63	53	Overall		0.309
						M vs. L	3.09 (0.53,18.11)	0.211
						H vs. L	1.11 (0.13,9.31)	0.920
	Enlisted Groundcrew	n	146	157	139	Overall		0.687
						M vs. L	1.21 (0.41,3.56)	0.724
						H vs. L	0.73 (0.22,2.41)	0.606
FVC	Officer	n	129	124	125	Overall		0.884
		Adj. Mean	91.0	90.8	91.6	M vs. L	--	0.902
		95% C.I.	(85.7,96.3)	(85.6,96.0)	(86.3,96.9)	H vs. L	--	0.725
	Enlisted Flyer	n	54	63	53	Overall		0.258
		Adj. Mean	93.6	90.4	90.1	M vs. L	--	0.157
		95% C.I.	(88.3,98.9)	(85.5,95.2)	(85.0,95.3)	H vs. L	--	0.147
	Enlisted Groundcrew	n	147	158	140	Overall		0.998**
		Adj. Mean**	90.4	90.3	90.3	M vs. L	--	0.960**
		95% C.I.**	(87.9,92.9)	(87.8,92.8)	(87.7,92.9)	H vs. L	--	0.951**

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
FEV ₁	Officer	n	129	124	125	Overall		0.464
		Adj. Mean	92.4	91.4	93.7	M vs. L	--	0.595
		95% C.I.	(86.4,98.4)	(85.5,97.2)	(87.7,99.6)	H vs. L	--	0.485
	Enlisted Flyer	n	54	63	53	Overall		0.925
		Adj. Mean	88.7	89.1	89.8	M vs. L	--	0.885
		95% C.I.	(82.0,95.3)	(83.0,95.1)	(83.4,96.3)	H vs. L	--	0.697
	Enlisted Groundcrew	n	147	158	140	Overall		0.322**
		Adj. Mean**	94.1	92.4	91.5	M vs. L	--	0.319**
		95% C.I.**	(91.1,97.0)	(89.4,95.4)	(88.4,94.6)	H vs. L	--	0.141**
FEV ₂	Officer	n	129	124	125	Overall		0.622
		Adj. Mean	89.8	89.3	90.9	M vs. L	--	0.747
		95% C.I.	(84.3,95.4)	(83.9,94.7)	(85.5,96.4)	H vs. L	--	0.528
	Enlisted Flyer	n	54	63	53	Overall		0.974
		Adj. Mean	88.5	88.0	88.0	M vs. L	--	0.844
		95% C.I.	(82.7,94.3)	(82.7,93.3)	(82.3,93.6)	H vs. L	--	0.840
	Enlisted Groundcrew	n	147	158	140	Overall		0.595**
		Adj. Mean**	90.9	89.9	89.4	M vs. L	--	0.499**
		95% C.I.**	(88.2,93.6)	(87.2,92.6)	(86.6,92.2)	H vs. L	--	0.319**

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
FEV ₃	Officer	n	129	124	125	Overall		0.745
		Adj. Mean	89.2	89.0	90.2	M vs. L	--	0.903
		95% C.I.	(83.9, 94.6)	(83.8, 94.3)	(84.9, 95.5)	H vs. L	--	0.554
	Enlisted Flyer	n	54	63	53	Overall		0.827
		Adj. Mean	89.5	88.3	88.1	M vs. L	--	0.619
		95% C.I.	(83.9, 95.0)	(83.3, 93.3)	(82.7, 93.4)	H vs. L	--	0.571
	Enlisted Groundcrew	n	147	158	140	Overall		0.778**
		Adj. Mean**	90.4	89.7	89.3	M vs. L	--	0.630**
		95% C.I.**	(87.7, 93.0)	(87.0, 92.3)	(86.6, 92.1)	H vs. L	--	0.491**
FEFmax	Officer	n	129	124	125	Overall		0.637**
		Adj. Mean**	136.4	136.4	138.8	M vs. L	--	0.982**
		95% C.I.**	(126.9, 145.9)	(127.1, 145.7)	(129.4, 148.3)	H vs. L	--	0.406**
	Enlisted Flyer	n	54	63	53	Overall		0.238
		Adj. Mean	129.9	136.4	137.2	M vs. L	--	0.155
		95% C.I.	(119.2, 140.6)	(126.7, 146.2)	(126.8, 147.6)	H vs. L	--	0.128
	Enlisted Groundcrew	n	147	158	140	Overall		0.164**
		Adj. Mean**	138.0	133.8	133.4	M vs. L	--	0.116**
		95% C.I.**	(133.3, 142.7)	(129.1, 138.6)	(128.5, 138.3)	H vs. L	--	0.088**

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Ratio of Observed FEV ₁ to Observed FVC	Officer	n	129	124	125	Overall		0.203
		Adj. Mean ^b	0.818	0.812	0.825	M vs. L	--	0.445
		95% C.I. ^b	(0.793, 0.840)	(0.787, 0.834)	(0.802, 0.846)	H vs. L	--	0.313
	Enlisted Flyer	n	54	63	53	Overall		0.071
		Adj. Mean ^b	0.774	0.800	0.807	M vs. L	--	0.078
		95% C.I. ^b	(0.734, 0.807)	(0.768, 0.827)	(0.774, 0.835)	H vs. L	--	0.030
	Enlisted Groundcrew	n	147	158	140	Overall		0.113
		Adj. Mean ^b	0.838	0.830	0.824	M vs. L	--	0.208
		95% C.I. ^b	(0.827, 0.849)	(0.818, 0.841)	(0.811, 0.836)	H vs. L	--	0.038

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Loss of Vital Capacity	Officer	n	130	124	124	Overall		0.272
						M vs. L ^c	1.41 (0.56, 3.57)	0.465
						H vs. L ^c	1.04 (0.40, 2.69)	0.943
						M vs. L ^d	0.45 (0.12, 1.73)	0.244
						H vs. L ^d	-- ^a	-- ^a
	Enlisted Flyer	n	55	63	53	Overall		0.895
						M vs. L ^c	1.26 (0.36, 4.43)	0.716
						H vs. L ^c	1.33 (0.37, 4.82)	0.663
						M vs. L ^d	0.41 (0.05, 3.20)	0.392
						H vs. L ^d	-- ^a	-- ^a
	Enlisted Groundcrew	n	146	157	139	Overall		0.406
						M vs. L ^c	1.11 (0.51, 2.41)	0.800
						H vs. L ^c	1.12 (0.53, 2.38)	0.764
						M vs. L ^d	2.19 (0.70, 6.90)	0.181
						H vs. L ^d	0.65 (0.17, 2.55)	0.541

TABLE 20-10. (continued)

Adjusted Exposure Index for Pulmonary Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Obstructive Abnormality	Officer	n	130	124	124	Overall		0.341
						M vs. L ^c	1.71 (0.94,3.13)	0.080
						H vs. L ^c	1.34 (0.73,2.47)	0.342
						M vs. L ^d	0.72 (0.24,2.18)	0.566
						H vs. L ^d	0.61 (0.19,1.89)	0.388
	Enlisted Flyer	n	55	63	53	Overall		0.274
						M vs. L ^c	0.45 (0.20,1.01)	0.054
						H vs. L ^c	0.53 (0.23,1.19)	0.124
						M vs. L ^d	0.61 (0.19,1.91)	0.397
						H vs. L ^d	0.42 (0.12,1.52)	0.186
	Enlisted Groundcrew	n	146	157	139	Overall		0.378
						M vs. L ^c	1.23 (0.67,2.26)	0.503
						H vs. L ^c	1.67 (0.93,2.99)	0.085
						M vs. L ^d	1.78 (0.50,6.28)	0.372
						H vs. L ^d	2.11 (0.69,6.50)	0.192

**Group-by-covariate interaction ($0.01 < p \leq 0.05$)--mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

--^aAdjusted relative risk/confidence interval/p-value not given due to a cell with zero frequency.

--Adjusted relative risk not applicable for continuous analysis of a variable.

^bTransformed from natural logarithm (1-X) scale.

^cMild contrasted with none.

^dModerate/severe contrasted with none.

TABLE 20-11.

**Summary of Exposure Index-by-Covariate Interactions
From Adjusted Analyses for Pulmonary Variables***

Variable	Occupation	Covariate	p-Value
Pleurisy	Enlisted Groundcrew	Current Cigarette Smoking	0.031
		Lifetime Cigarette Smoking History	0.045
Pneumonia	Officer	Lifetime Cigarette Smoking History	0.048
Pneumonia	Enlisted Flyer	Race	0.017
Hyperresonance	Officer	Lifetime Cigarette Smoking History	0.028
Hyperresonance	Enlisted Groundcrew	Age	0.033
Wheezes	Enlisted Groundcrew	Age	0.014
FVC	Enlisted Groundcrew	Lifetime Cigarette Smoking History	0.012
FEV ₁	Enlisted Groundcrew	Lifetime Cigarette Smoking History	0.038
FEV ₂	Enlisted Groundcrew	Lifetime Cigarette Smoking History	0.022
FEV ₃	Enlisted Groundcrew	Lifetime Cigarette Smoking History	0.019
FEFmax	Officer	Lifetime Cigarette Smoking History	0.049
FEFmax	Enlisted Groundcrew	Race	0.016

*Refer to Table Q-3 for a further investigation of these interactions.

Bronchitis

The unadjusted analyses of bronchitis revealed no significant differences among the exposure categories for officers and enlisted groundcrew. These results were supported by the adjusted analyses.

Based on the unadjusted analysis, a significant difference was detected for the enlisted flyers ($p=0.003$). For the enlisted flyer cohort, 32.7 percent of the low exposure category reported having had bronchitis, as contrasted with 7.9 percent and 18.9 percent of the medium and high exposure categories, respectively. The medium versus low contrast was significant (Est. RR: 0.18, 95% C.I.: [0.06,0.52], $p=0.001$). The same pattern was found in the adjusted analysis. The overall test for enlisted flyers was significant in the adjusted analysis ($p=0.003$). Based on the adjusted analysis of the contrasts, the Ranch Hands in the medium exposure category were significantly different than those in the low exposure category for bronchitis (Adj. RR: 0.18, 95% C.I.: [0.06,0.53], $p=0.001$). These results are opposite of an expected herbicide effect and do not support a dose-response relationship.

Pleurisy

There were no significant differences detected in the unadjusted exposure index analyses of pleurisy. These results were supported by the adjusted analyses for the officer and enlisted flyer cohorts.

In the enlisted groundcrew cohort, the interactions involving exposure index were significant for current cigarette smoking and lifetime cigarette smoking history ($p=0.031$ and $p=0.045$, respectively). When the interactions were investigated by stratifying by current and lifetime cigarette smoking, there were sparse numbers of participants reporting an occurrence of pleurisy in many of the strata. The overall test for the former smokers who were classified as moderate lifetime smokers was borderline significant ($p=0.063$). Of the enlisted groundcrew in this stratum, 17.6 percent of those in the low exposure category reported having had pleurisy, as contrasted to 0.0 percent and 5.3 percent in the medium and high exposure categories, respectively. The medium versus low and high versus low contrasts were not significant. There were no significant differences in the enlisted groundcrew cohort in the adjusted analysis without the interactions involving exposure index in the model.

Pneumonia

No significant differences in the occurrence of pneumonia among the exposure categories were identified in the unadjusted analyses. In the adjusted analysis of the officer cohort, there was a significant exposure index-by-lifetime cigarette smoking history interaction ($p=0.048$). After stratifying by lifetime cigarette smoking, there were no significant differences identified. For the enlisted flyer cohort, there was a

significant exposure index-by-race interaction ($p=0.017$). No significant differences were identified for nonblacks. One Black enlisted flyer in the low exposure category reported an occurrence of pneumonia ($p=0.018$). No other participants in this category reported pneumonia. The medium versus low and high versus low exposure contrasts for the Black enlisted flyers were not significant. Without the significant interactions in the models, no differences were detected for either the officer or enlisted flyer cohorts. There were also no significant differences found in the enlisted groundcrew cohort based on the adjusted analyses.

Tuberculosis

Based on the unadjusted analyses, there were no significant differences found for tuberculosis. Due to the low number of Ranch Hands who reported having had tuberculosis, adjusted exposure index analyses were not conducted.

Physical Examination Variables

Thorax and Lung Abnormalities

The unadjusted exposure index analyses of thorax and lung abnormalities did not reveal any significant differences. The adjusted analyses supported this finding for the enlisted flyer and enlisted groundcrew cohorts. For the officer cohort, the overall result of the adjusted analysis was borderline significant ($p=0.067$). For the officers, the percentage of abnormalities was 6.9, 5.6, and 2.4 for the low, medium, and high exposure categories, respectively. In the adjusted analysis, the high versus low contrast was significant (Adj. RR: 0.20, 95% C.I.: [0.04, 0.93], $p=0.040$). Since the percentage of abnormalities decreased as exposure increased, the results do not suggest a dose-response relationship.

Asymmetric Expansion

There were no Ranch Hands with an asymmetric expansion. Thus, no exposure index analyses for this variable were performed.

Hyperresonance

No significant differences were detected in the unadjusted analyses of hyperresonance. Based on the adjusted analyses, there were no differences found for the enlisted flyer cohort. In the officer cohort, there was a significant exposure index-by-lifetime cigarette smoking history interaction ($p=0.028$); stratifying by the lifetime cigarette smoking history categories revealed no significant differences. The exposure index-by-age interaction was significant in the adjusted analysis of the enlisted groundcrew cohort ($p=0.033$); however, no differences were found after stratifying by age. Without the significant interactions in the models, there were no significant differences detected for either the officer or enlisted groundcrew cohorts.

Dullness

Only two Ranch Hands had dullness on examination of the lungs: one enlisted flyer in the medium exposure category and one enlisted groundcrew in the low exposure category. No significant differences were identified in unadjusted analyses. Due to the small number of occurrences of dullness, no adjusted analyses were performed on this variable.

Wheezes

In the unadjusted analyses, there were no significant differences detected. This finding was supported by the results of the adjusted analyses for the officer and enlisted flyer cohorts. For the enlisted groundcrew cohort, there was a significant exposure index-by-age interaction ($p=0.014$). No significant differences were identified after stratifying by age. Without the interaction in the adjusted model, no difference among the exposure categories was revealed.

Rales

In the unadjusted and adjusted exposure index analyses of rales, no significant differences were identified.

X-Ray Interpretation

The results of the unadjusted and adjusted analyses of x-ray abnormalities did not reveal any significant differences.

Laboratory Examination Variables

FVC

There was no evidence of a significant dose-response relationship based on the unadjusted analyses of FVC. The results of the adjusted analyses were consistent with the unadjusted results for the officer and enlisted flyer cohorts.

For the enlisted groundcrew, there was a significant exposure index-by-lifetime cigarette smoking history interaction ($p=0.012$). After stratifying by lifetime cigarette smoking history, one contrast, medium versus low, was borderline significant for nonsmokers ($p=0.084$). The adjusted mean of the nonsmokers in the medium exposure category within the enlisted groundcrew cohort was 88.6 percent, as contrasted to an adjusted mean of 93.5 percent for the low exposure category; the adjusted mean of the high exposure category was 90.1 percent. No significant difference was detected in the enlisted groundcrew cohort based on an analysis without the exposure index-by-lifetime cigarette smoking history interaction.

FEV₁

No significant dose-response relationship for FEV₁ was detected in the unadjusted exposure index analyses. This finding was supported by the adjusted results for the officer and enlisted flyer cohorts.

In the enlisted groundcrew cohort there was a significant exposure index-by-lifetime cigarette smoking history interaction ($p=0.038$). Stratifying by this covariate identified one borderline significant contrast: high versus low exposure for the moderate lifetime smokers ($p=0.079$). The adjusted mean of the high exposure category within that stratum was 89.1 percent, as contrasted to an adjusted mean of 94.8 percent for the low exposure category. The adjusted mean of the medium exposure category for the same stratum was 92.4 percent. Without the exposure index-by-covariate interaction, no significant difference was detected.

FEV₂

The unadjusted analyses of FEV₂ failed to detect any significant dose-response relationships. Similarly, in the adjusted analyses, no significant differences were found for the officer and enlisted flyer cohorts. In the enlisted groundcrew cohort, there was a significant interaction involving exposure index for lifetime cigarette smoking history ($p=0.022$). Investigation of the interaction by stratifying did not reveal any significant contrasts. Without the exposure index-by-covariate interaction in the model, no difference within the enlisted groundcrew cohort was found.

FEV₃

For the three occupational cohorts, no significant dose-response relationships were identified in the unadjusted analyses of FEV₃. The adjusted analyses also did not reveal any significant differences for the officer and enlisted flyer cohorts.

Within the enlisted groundcrew cohort, the exposure index-by-lifetime cigarette smoking history interaction was significant ($p=0.019$). As with FEV₁ and FEV₂, FEV₃ adjusted means decreased as exposure increased for the moderate lifetime smoker strata. Further investigation of the interaction by stratifying by the covariate did not identify any significant differences, however. Without the interaction in the model, no significant dose-response relationship was revealed.

FEFmax

For the officer cohort, no significant differences were detected in the unadjusted analyses of FEFmax. In the adjusted analyses, there was a significant exposure index-by-lifetime cigarette smoking history interaction ($p=0.049$). One borderline significant contrast, high versus low exposure within the heavy smokers, was found ($p=0.057$). The adjusted mean of the high exposure category was 139.9 percent, as contrasted to an adjusted mean of 130.8 percent for the low exposure category within the officers classified as

heavy lifetime cigarette smokers. This finding was opposite of an expected herbicide effect and did not support an increasing dose-response relationship. The corresponding adjusted mean for the medium exposure category was 129.4 percent. Without the interaction in the model, no significant difference was found.

In the unadjusted analyses of the enlisted flyer cohort, the high versus low exposure contrast was borderline significant ($p=0.076$). The means of the low, medium, and high exposure categories for the enlisted flyer cohort were 128.3 percent, 136.7 percent, and 137.5 percent, respectively. No significant differences were detected in the adjusted analyses of this cohort.

In the enlisted groundcrew cohort, the unadjusted analyses revealed a borderline difference between the high and low exposure categories (136.1% for low vs. 130.7% for high, $p=0.064$; 133.5% for medium). In the adjusted analyses, there was a significant exposure index-by-race interaction ($p=0.016$). Stratifying by race, the high versus low exposure contrasts were significant for both Blacks and nonblacks ($p=0.028$ and $p=0.012$, respectively). The medium versus low exposure contrasts for nonblack enlisted groundcrew were borderline significant ($p=0.066$). The adjusted means of the low, medium, and high exposure categories for Black enlisted groundcrew were 130.6 percent, 134.2 percent, and 149.9 percent, respectively. For the nonblack enlisted groundcrew, the adjusted means were 137.2 percent, 132.1 percent, and 130.0 percent for the low, medium, and high exposure categories, respectively. Without the significant interaction in the model, the high versus low exposure contrast was borderline significant (adjusted means: 138.0% for low, 133.8% for medium, and 133.4% for high; $p=0.088$).

Ratio of Observed FEV₁ to Observed FVC

In the unadjusted and adjusted exposure index analyses of the officer cohort, no significant dose-response relationship was identified for the ratio of observed FEV₁ to observed FVC.

The means of the enlisted flyer cohort for the low, medium, and high exposure categories were 0.772, 0.805, and 0.810, respectively. In the unadjusted analysis, the overall, medium versus low, and high versus low contrasts were significant ($p=0.037$, $p=0.043$, and $p=0.016$, respectively). In the adjusted analysis, the high versus low contrast was significant ($p=0.030$), and the overall and medium versus low contrasts were borderline significant ($p=0.071$ and $p=0.078$, respectively). The adjusted means for the low, medium, and high exposure categories were 0.774, 0.800, and 0.807, respectively.

For the enlisted groundcrew cohort, the unadjusted analysis revealed that the overall and the high versus low exposure contrasts were significant ($p=0.047$ and $p=0.020$, respectively). The means of the enlisted groundcrew cohort for the low, medium, and high exposure categories were 0.831, 0.828, and 0.813, respectively. Based on the adjusted analysis, the high versus low exposure contrast was significant ($p=0.038$). The adjusted means were 0.838, 0.830, and 0.824 for the low, medium, and high exposure categories, respectively.

Loss of Vital Capacity

In the exposure index analyses for loss of vital capacity, there are three exposure categories and three categories of loss of vital capacity (none, mild, and moderate/severe). Consequently, an overall assessment of these nine categories was made, as well as four individual contrasts for each occupational stratum. In particular, medium versus low and high versus low exposure contrasts were examined for both the mild versus none and the moderate/severe versus none loss of vital capacity categories.

In the high versus low exposure contrast for the officer cohort, a borderline significant difference was detected for the moderate/severe loss of vital capacity versus none contrast based on the unadjusted analysis ($p=0.069$). Five officers in the low exposure category had a moderate or severe loss of vital capacity, as compared to zero officers in the high exposure category with a moderate or severe loss of vital capacity. There were 117 officers with no loss of vital capacity in the low exposure category, as compared to 115 in the high exposure category.

Neither the unadjusted nor adjusted analyses revealed any significant differences among the exposure categories for enlisted flyers or enlisted groundcrew.

Obstructive Abnormality

As with loss of vital capacity, obstructive abnormality was also classified as none, mild, or moderate/severe. For the unadjusted exposure index analyses of the officer cohort, significant or borderline significant differences were found for both the medium versus low ($p=0.016$) and the high versus low ($p=0.075$) exposure contrasts for mild versus none obstructive abnormality. The estimated relative risk for the medium versus low contrast was 2.09 (95% C.I.: [1.18, 3.70]) and 1.76 for the high versus low contrast (95% C.I.: [0.99, 3.13]). The medium versus low contrast was borderline significant in the adjusted analysis (Adj. RR: 1.71, 95% C.I.: [0.94, 3.13], $p=0.080$).

In the unadjusted analysis of the medium versus low exposure contrast for the enlisted flyer cohort, a borderline significant difference was detected for the mild versus none obstructive abnormality contrast (Est. RR: 0.46, 95% C.I.: [0.21, 1.03], $p=0.089$). A borderline significant difference was also found in the adjusted analysis (Adj. RR: 0.45, 95% C.I.: [0.20, 1.01], $p=0.054$).

For the enlisted groundcrew cohort, a borderline significant difference was detected in the overall assessment based on the unadjusted analysis ($p=0.096$). In the high versus low exposure contrast, a borderline significant difference was found for the mild versus none obstructive abnormality contrast (Est. RR: 1.75, 95% C.I.: [0.99, 3.10], $p=0.072$). This contrast was also borderline significant based on the adjusted analysis (Adj. RR: 1.67, 95% C.I.: [0.93, 2.99], $p=0.085$). These results were suggestive of a dose-response relationship, although no other contrasts were significant.

TABLE 20-12.

Longitudinal Analysis of Ratio of Observed FEV₁ to Observed FVC:
A Contrast of 1982 Baseline and 1987 Followup Examination Means

Examination	Group Means*		p-Value (Equality of Differences)
	Ranch Hand	Comparison	
1982 Baseline	0.813	0.815	0.789
1987 Followup	0.814	0.815	

*Means transformed from the natural logarithm (1-X) scale; hypothesis test performed on the natural logarithm (1-X) scale.

Note: Summary statistics for the 1982 Baseline and the 1987 followup are based on 942 Ranch Hands and 1,110 Comparisons who participated in the 1982 Baseline and the 1987 followup examinations. Two Comparisons were excluded from the analysis due to ratios greater than 1.0 at the 1982 Baseline examination.

Longitudinal Analysis

The ratio of observed FEV₁ to observed FVC was investigated for the longitudinal analysis of the pulmonary function. Results, summarized in Table 20-12, showed that the group difference did not change significantly between the 1982 Baseline and the 1987 followup examination (p=0.789).

Mortality Data

Based on the 31 December 1987 mortality data, there were 22 deaths (0.05/1,000 person-years) from respiratory conditions in the Comparison group and none in the Ranch Hand group. There were 1,261 Ranch Hands and 19,101 Comparisons in this mortality analysis.

DISCUSSION

While the presence of pulmonary disease is often evident based on a careful history and physical examination, definitive diagnosis usually requires the collection of data from a number of other sources. The standard radiographic examination of the chest and pulmonary function studies are routinely ordered and were included as variables in the Air Force Health Study examination. In addition, because the lung is often involved secondarily in numerous infectious, inflammatory, and neoplastic disorders, the assessment of pulmonary disease should include the type of comprehensive multisystem review conducted in this examination cycle and reported in other chapters.

Historical information on the occurrence of pulmonary disease must be interpreted with caution in the absence of medical record verification. Many of the cardinal symptoms of lung disease, including dyspnea, chest pain, and exercise intolerance, are common to cardiovascular disease as well (particularly ischemic heart disease) and are frequently misinterpreted as to cause. Wheezing, assumed by the patient to be indicative of asthma, may in fact be reflective of hemodynamic compromise in congestive heart failure. A positive purified protein derivative skin test, indicative of subclinical tuberculous infection, may be erroneously interpreted and reported as prior active infection. "Pneumonia" and "pneumonitis" are often confused by patients in relating the medical history.

The physical examination variables studied can provide valuable clues to the presence of pulmonary disease. In lacking specificity, however, these data are often of limited utility in confirming a specific diagnosis. Wheezes and hyperresonance, for example, will occur in obstructive airway disease in asthma or in emphysema secondary to cigarette use. Dullness to percussion, a finding common to many disorders, will occur in consolidation from atelectasis, infections, pleural thickening, or pleural effusion.

In view of the limitations of the history and physical examination noted above, added emphasis is placed on screening laboratory data in the diagnosis of respiratory disease. The chest x ray, when normal, is highly reliable in excluding pulmonary parenchymal disease, though several exceptions must be recognized. Solitary lesions less than 6 millimeters, miliary granulomatous infection, and early interstitial disease, among others, may be present but not detectable radiographically. On the other hand, the chest x ray may reveal an early occult malignancy in an asymptomatic patient and thus afford an opportunity for cure.

Spirometry has been used as a clinical tool to measure static lung volumes and to detect respiratory disease for over a century. Dynamic indices, relating changes in lung volume to time, were first developed over 50 years ago and, with computerization, have been refined to a high degree of accuracy and reproducibility. To be valid, spirometry requires that particular attention be paid to technician training and, with proper coaching, to eliciting the full cooperation of the patient. In any longitudinal study emphasis must be placed on the use of identical techniques to ensure comparability of data.

In broad terms, the spirometric indices evaluated in this chapter are designed to measure lung volume (vital capacity) and respiratory air flow (FEV). Static lung volume is principally determined by height and is independent of weight, while dynamic volume measurements depend in part on physical strength. Accordingly, all indices require correction for age and gender. Further, as confirmed in the present study, normal values for Whites cannot be applied to other ethnic groups.

In clinical practice, respiratory disease can be divided into two broad categories. "Restrictive" disease is characterized by reduced vital capacity as seen in interstitial fibrosis or reduced lung volume after surgical resection. In "obstructive" airways disease, usually emphysema associated with cigarette use, there is abnormal prolongation of the flow-dependent indices (FEV_1 , FEV_2 , FEV_3 , and PEF_{max}).

With few exceptions, the dependent variable-covariate associations found in the statistical analyses, confirm observations that are well established in clinical practice. With advancing age, an increased incidence of respiratory disease would be expected and was confirmed by history, on physical examination, and in the laboratory. The age-related decline in vital capacity is considered "physiologic" over time and will occur independent of acquired pulmonary disease.

The cause of the increased incidence of bronchitis and pneumonia in nonblacks is uncertain and cannot be explained on the basis of any previously established genetic or ethnic susceptibility. Differential access and use of medical care may play a role. In contrast, Blacks were found to be at detriment by all spirometric indices.

In the exposure index analyses, the ratio of FEV₁ to FVC revealed similar trends in the enlisted flyer and enlisted groundcrew cohorts. Although the data may reflect some herbicide-related health detriment, two confounding variables must be taken into consideration. As an index reflective of obstructive airways disease, the FEV₁ will diminish with increased cigarette smoking over time. Secondly, as an effort-dependent index, the FVC is subject to performance bias and requires a fully compliant participant in order to be valid. Even in those studies considered technically adequate, the self-perception of prior herbicide exposure could introduce subtle bias sufficient to affect the results. It will be important to reexamine the FEV₁/FVC ratio data when the body burden of herbicide can be defined more objectively by serum levels.

As expected, current and lifetime cigarette use were associated with significant abnormalities in all variables examined. Enlisted participants, with greater lifetime and current cigarette exposure, were at detriment relative to officers.

Finally, though limited to a single variable, the longitudinal analysis revealed no significant difference in the Ranch Hands versus the Comparisons. These observations will be greatly strengthened by longitudinal analysis of the spirometric variables in future examination cycles.

In summary, data collected in the pulmonary assessment provide a valid reflection of lung function in the population under study. There was a similar incidence of respiratory disease and similar respiratory function in the Ranch Hand and Comparison groups.

SUMMARY

The 1987 pulmonary assessment was based on five questionnaire variables, seven variables from the physical examination, and eight laboratory variables. The results of the Ranch Hand and Comparison contrasts are summarized in Table 20-13.

The five questionnaire variables were based on self-reported data for the occurrence of the following conditions: asthma, bronchitis, pleurisy, pneumonia, and tuberculosis. There were no differences identified between the Ranch Hands and the Comparisons based on the unadjusted analyses. The results

TABLE 20-13.

**Overall Summary Results of Unadjusted and Adjusted
Group Contrast Analyses of Pulmonary Variables**

Variable	Type of Analysis	Unadjusted	Adjusted	Direction of Results
<u>Questionnaire</u>				
Asthma	D	NS	NS	
Bronchitis	D	NS	NS	
Pleurisy	D	NS	NS	
Pneumonia	D	NS	****	
Tuberculosis	D	NS	--	
<u>Physical Examination</u>				
Thorax and Lung Abnormalities	D	0.020	NS*	RH>C
Asymmetric Expansion	D	NS	--	
Hyperresonance	D	NS*	** (NS)	RH>C
Dullness	D	NS	--	
Wheezes	D	NS	NS	
Rales	D	NS	NS	
X-Ray Interpretation	D	NS	** (NS)	
<u>Laboratory</u>				
FVC	C	NS	NS	
FEV ₁	C	NS	** (NS)	
FEV ₂	C	NS	** (NS)	
FEV ₃	C	NS	NS	
PEFmax	C	NS	NS	
Ratio of Observed FEV ₁ to Observed FVC	C	NS	NS	
Loss of Vital Capacity	D	NS	NS	
Obstructive Abnormality	D	NS	NS	

D: Discrete analysis performed.

NS: Not significant ($p > 0.10$).

****: Group-by-covariate interaction ($p < 0.01$); refer to Table Q-2 for a detailed description of this interaction.

--Analysis not performed.

NS*: Borderline significant ($0.05 < p < 0.10$).

RH>C: Higher prevalence rate in Ranch Hands than in Comparisons.

** (NS): Group-by-covariate interaction ($0.01 < p < 0.05$); not significant when interaction is deleted; refer to Table Q-2 for a detailed description of this interaction.

C: Continuous analysis performed.

of the adjusted analyses supported this finding for asthma, bronchitis, and pleurisy. Due to the low number of participants reporting tuberculosis, no adjusted analysis was conducted. In the adjusted analysis of pneumonia, there was a significant interaction between group and lifetime cigarette smoking history ($p=0.004$). Stratifying by the covariate showed that a significantly higher percentage of Comparisons in the heavy cigarette smoking category reported pneumonia than heavy smoking Ranch Hands ($p=0.005$).

The physical examination variables of the pulmonary assessment were: thorax and lung abnormalities, asymmetric expansion, hyperresonance, dullness, wheezes, rales, and x-ray interpretation.

The Ranch Hands had significantly more thorax and lung abnormalities than the Comparisons based on the unadjusted analysis ($p=0.020$). After adjusting for age, occupation, current cigarette smoking, and lifetime cigarette smoking history, the difference was borderline significant ($p=0.072$).

There was only one participant--a Comparison--with asymmetric expansion. No significant difference was detected in the unadjusted analysis, and due to the low number of participants with this condition, no adjusted analysis was conducted.

The unadjusted analysis of hyperresonance showed a borderline difference between the two groups with a higher prevalence rate among the Ranch Hands ($p=0.100$). In the adjusted analysis, there was a significant group-by-occupation interaction ($p=0.017$). Stratifying by occupation revealed that the Ranch Hand enlisted flyers had a significantly higher rate of hyperresonance than the Comparison enlisted flyers ($p=0.006$). Without the group-by-occupation interaction in the model, no difference between the two groups was detected.

There was a total of three participants diagnosed with dullness of the lungs: two Ranch Hands and one Comparison. No difference was found in the unadjusted analysis. Due to the low prevalence rate of dullness, no adjusted analysis was performed.

Neither the unadjusted nor adjusted analyses for wheezes and rales detected a difference between the Ranch Hands and the Comparisons.

No significant difference between the two groups was identified based on the unadjusted analysis of x-ray abnormalities. In the adjusted analysis, there was a significant group-by-race interaction ($p=0.023$). Exploring the interaction by stratifying on race showed a borderline significant difference between the Black Ranch Hands and the Black Comparisons, with the Ranch Hands having more x-ray abnormalities ($p=0.068$). Without the interaction in the model, no significant difference was found.

The eight laboratory variables of the pulmonary assessment were: FVC, FEV_1 , FEV_2 , FEV_3 , FEFmax, ratio of observed FEV_1 to observed FVC, loss of vital capacity, and obstructive abnormality. For six of the eight variables, no significant difference was detected between the Ranch Hands and the Comparisons in both the unadjusted and adjusted analyses. These six variables were: FVC, FEV_3 , FEFmax, ratio of observed FEV_1 to observed FVC, loss of vital capacity, and obstructive abnormality.

No significant difference was identified in the unadjusted analysis of FEV_1 . This result was supported by the adjusted analysis without the significant group-by-age interaction ($p=0.037$). When the interaction was explored, the Ranch Hands born between 1923 and 1941 were found to have a significantly lower adjusted mean than the Comparisons in the same age category ($p=0.022$). However, the Ranch Hands who were born in or before 1922 had a marginally higher adjusted mean than the Comparisons in that category ($p=0.081$).

The results of the analyses of FEV_2 were similar to the results of FEV_1 . No difference between the two groups was detected based on the unadjusted analysis. In the adjusted analysis, there was a significant interaction between group and age ($p=0.042$). Of the participants born between 1923 and 1941, the Ranch Hands had a significantly lower adjusted mean FEV_2 than the Comparisons ($p=0.017$). Among the participants who were born in or before 1922, a borderline significant group difference was found with the adjusted mean of the Comparisons being lower than the adjusted mean of the Ranch Hands ($p=0.070$).

Although the results were primarily not significant or borderline significant, the relative risk was greater than 1 or the mean of the Ranch Hands was less favorable than the mean of the Comparisons in 17 of the 20 unadjusted analyses. In general, this pattern was repeated in the adjusted analyses, where the models were adjusted for the effects of cigarette smoking; again, however, the results were primarily not significant. Trends such as these are discussed in Chapter 21.

Longitudinal analyses showed no changes over time between groups for the ratio of observed FEV_1 to observed FVC. The exposure index analyses detected significant results suggestive of a dose-response relationship infrequently, and no pattern in the results emerged. Exposure index-by-covariate interactions observed were primarily with the two smoking covariates.

In conclusion, 14 variables demonstrated nonsignificant results in both unadjusted and adjusted Ranch Hand versus Comparison group contrasts. Two variables exhibited a significant or borderline significant result affecting the Ranch Hands in either the unadjusted or adjusted analyses. The Ranch Hands had more thorax and lung abnormalities than the Comparisons based on the unadjusted analysis; after adjustment for age and current cigarette smoking, the difference was borderline significant. A borderline significant difference in hyperresonance was found in the unadjusted analysis, and a group-by-occupation interaction was present in the adjusted analysis. Four additional variables were nonsignificant in unadjusted analyses with a group-by-covariate interaction present in the adjusted analyses. Of the five interactions, two variables showed a significant detriment to the Ranch Hands, one a significant detriment to the Comparisons, and two variables demonstrated mixed results; that is, significant or borderline significant results were present for both Ranch Hands and Comparisons, depending on which covariate stratum was examined. Without the group-by-covariate interactions in the final model, no significant effects due to group were seen. Although the pulmonary health of the two groups was reasonably comparable, assessment of the pulmonary function should be included in the future examinations.

CHAPTER 20

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